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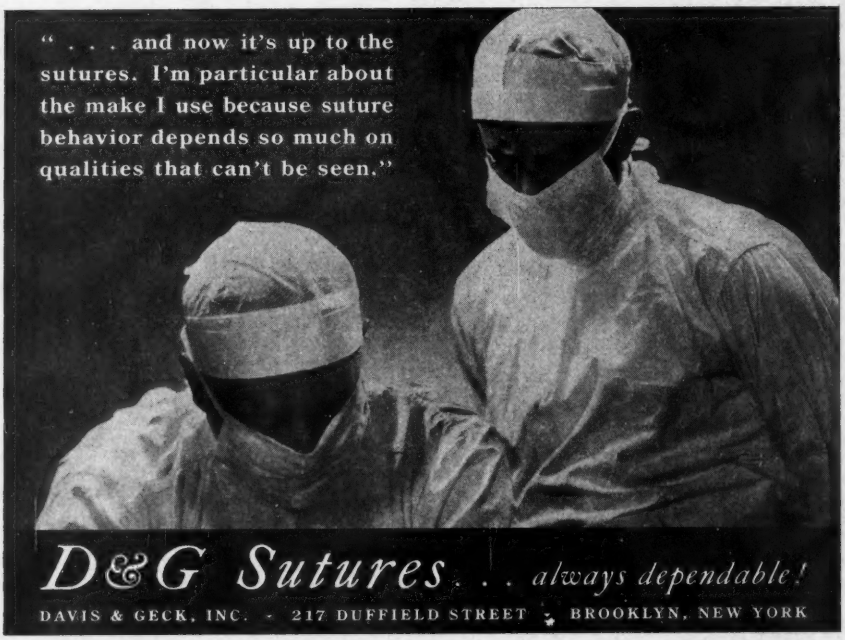
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The Journal of Thoracic Surgery

VOL. 4 DECEMBER, 1934 NO. 2

Original Communications

MALIGNANT DISEASE OF THE LUNG*

A. TUDOR EDWARDS, M.D., M.CHIR., F.R.C.S., LONDON, ENGLAND

Surgeon to the Brompton Hospital for Diseases of the Chest

THE largely increasing number of patients diagnosed as suffering from malignant disease of the lung during recent years is sufficient reason for a detailed consideration of the disease in all its aspects. Whether the increase is absolute or to a great extent determined by improved diagnostic methods is really of academic rather than practical interest; although survey of the literature of the subject is strongly suggestive that the absolute incidence of the disease in this region is steadily increasing. Many observers put the incidence of pulmonary cancers between 5 and 10 per cent of all carcinomas and others even higher. Obviously, if these figures are correct, it is our bounden duty to devote considerably more study to this disease in all its aspects in the future than has been done in the past and more especially with regard to early diagnosis; in this way some more determined attempts may be made to treat these conditions at a stage at which we are becoming accustomed to treat the more superficial forms of carcinoma.

Unfortunately, the onset in many cases is insidious, and in some cases it appears to arise in the lungs of individuals who have for many years been the victims of such chronic pulmonary disease as bronchitis or tuberculosis.

In others the condition arises in individuals who have a history peculiarly free from illness in any form. Furthermore, the enormous improvement in thoracic surgery particularly in this respect, pulmonary resection, justifies the hope that in the near future many patients who in the relatively recent past have been doomed when

*Read by special invitation before the Seventeenth Annual Meeting of the American Association for Thoracic Surgery at Boston, Mass., May 31, June 1 and 2, 1934.

the diagnosis is made, may be enabled to recover completely or at any rate to look forward to a distinct prolongation of life. For the above reasons it is advisable to consider the methods at our disposal and to determine their relative value.

I, therefore, propose to take for my purpose a series of 73 cases in which the patients have received some form of treatment, either radical operation, radon seeds into the bronchus or radon seeds directly into the growth following thoracotomy. This group does not include a further series of some 18 patients submitted to exploration but in which it was obvious that no treatment was likely to be of value or in which drainage of the pleura alone has been carried out in order to relieve the effect of empyema secondary to extensive pulmonary growth.

As a preliminary, I would mention one or two points about the etiology of the condition.

Sex.—In the series of 73 cases, 53 patients were men and 20 women. These figures show the preponderance of males which is apparently characteristic.

Age.—

20 to 30 years	2 patients.
30 to 40 years	9 patients.
40 to 50 years	24 patients.
50 to 60 years	24 patients.
60 to 70 years	14 patients.

The youngest patient was a man aged twenty-six years and the oldest a man aged sixty-nine years.

Side and Site.—The disease occurred on the *right* side in 33 and on the *left* side in 40 patients, showing a slight preponderance of left-sided lesions.

With regard to the site of the disease on the respective sides, the figures show the lesion to be situated in:

Left upper lobe or bronchus	14 cases.
Left lower lobe or bronchus	26 cases.
Right upper lobe or bronchus	6 cases.
Right middle lobe or bronchus	5 cases.
Right lower lobe or bronchus	20 cases.
Right hilar region	2 cases.

Occupation and Previous Chest Disease.—As far as can be determined at present, occupation does not appear to be of any etiologic importance; and, although the previous history often contains evidence of influenza, bronchitis and pleurisy, it is more than probable that these are the first signs of the malignant changes in the lung rather than actual predisposing factors.

SYMPTOMS

Cough was present in every case in the series except one and can, therefore, be considered an almost invariable symptom. In many cases it is nonproductive, being of a dry irritating type.

Sputum. There was a definite amount of regular expectoration which was generally of a mucoid, frothy type in 47 patients, i.e., 64 per cent. Occasionally the sputum is definitely purulent and may resemble that encountered in cases of bronchiectasis or pulmonary abscess.

Hemoptysis of a greater or lesser degree occurred in 64 cases, or 87.7 per cent of patients, and varied from a little staining to a brisk hemorrhage. Not rarely hemorrhage may be so profuse as to cause rapid death.

Dyspnea was present in 54 cases, or 74 per cent, and does not appear to depend upon the amount of lung tissue put out of action by the disease. This may be due to involvement of the branches of the vagus nerve or to toxic absorption, but no sufficient explanation has yet been advanced. Where large secondary effusions are present, the cause of dyspnea is obvious.

Paralysis of the diaphragm secondary to invasion of the phrenic nerve may be the cause of sudden increase in dyspnea. This symptom is occasionally accompanied by some degree of cyanosis.

Pain was variable but was present to a greater or lesser degree in 60 per cent of cases. It varied from an occasional feeling of discomfort to an intense neuritis due to the growth invading the chest wall and involving the intercostal nerves. It is interesting that in one patient in the series the first symptom drawing attention to the disease was the pain from spontaneous fracture of a rib actually invaded by the malignant growth.

Involvement of the recurrent laryngeal nerve by secondary deposits in the mediastinum may be the cause of partial loss of voice or hoarseness.

CLINICAL SIGNS

The clinical signs vary considerably according to the situation of the growth. Where the growth occurs in the main bronchus of a lobe, the signs will generally be those of bronchial obstruction causing atelectasis of the involved lobe. These consist of dullness on percussion over the affected area, absence of breath sounds, and generally increased vocal resonance associated with displacement of the mediastinum toward the affected side. In the lower lobes this can be determined clinically by the position of the heart's apex beat.

In the later stage of the disease there may be obvious evidence of a secondary pleural effusion with the well-recognized physical signs accompanying it. The effusions are often serous in type, particularly in the early, but are not rarely blood stained in the later stages.

In those cases in which the carcinoma arises in the more peripheral parts of the lung, probably arising in secondary or tertiary bronchi, physical signs may be absent or only be those of a relatively small localized area of dullness. Signs of involvement of the left recurrent laryngeal nerve as evidenced by loss of voice or hoarseness, or of the sympathetic by the appearance of Horner's syndrome in the left eye, strongly suggest the presence of secondary malignant disease involving the glands of the mediastinum in the region of the arch of the aorta and may be said to contraindicate any form of treatment to the local lesion. The supraclavicular and axillary regions should be examined for enlarged lymphatic glands and the abdomen for hepatic enlargement. Clubbing of fingers and toes is quite common; in fact the most marked case of this I have seen occurred in association with a pulmonary neoplasm, being the only evidence suggesting a thoracic lesion.

X-RAY EXAMINATION

This examination is essential in all patients in whom there is the faintest suspicion of carcinoma and in whom there is an unexplained hemoptysis.

In those carcinomas blocking the main bronchi or the commencement of the secondary bronchi, there will be visible on x-ray examination a triangular shadow with its apex directed to the hilum, corresponding to the area of lung blocked by the bronchial obstruction, the radiologic opacity resulting from the absorption of air from this portion of the lung.

Radiographic screen examination will determine the mobility of the diaphragm and will thereby give valuable information of the presence of secondary glands in the mediastinum involving the phrenic nerve on the affected side. In only one case of benign mediastinal growth —a large intrathoracic goiter—have I seen phrenic paralysis.

In growths arising outside the main bronchi the characteristic radiologic appearance is that of an opacity of relatively uniform density, often rounded in outline and sharply marked off from the surrounding lung. This generally serves to distinguish a malignant growth from pulmonary abscess in which the opacity tends to fade off gradually into the surrounding lung. However, greater difficulty in diagnosis may be encountered where the central portion of growth has broken down and liquefied, since in these cases a definite fluid level may be visible and secondary infection of the central area may make diagnosis by radiography alone impossible. In fact, in a series of cases of abscess of the lung published some two or three years ago, I found that 10 per cent of the cases operated upon as chronic pulmonary abscess were found to have arisen in an area of primary malignant disease.

BRONCHOGRAPHY

Radiologic examination after the introduction of lipiodol into the bronchi—the so-called bronchogram—is essential. This will give positive evidence of obstruction of the bronchi and of its situation. Further, it will distinguish partial obstruction caused by narrowing of the bronchial lumen from either within or without. Some observers even consider that it is possible by the appearances at the site of obstruction to distinguish lesions caused by malignant disease and those caused by stenosis following syphilitic ulceration of the bronchi. Of the latter diagnosis I am more than a little suspicious—the positive character of the Wassermann reaction in any patient is by no means diagnostic that the lesion under investigation is necessarily syphilitic. In patients with more peripheral growths, bronchograms may also be of considerable value as they may demonstrate lack of filling of the involved area with lipiodol.

BRONCHOSCOPY

The value of this diagnostic measure in suspected malignant disease of the bronchi cannot be overestimated. When the primary growth arises in the main bronchi or at the immediate commencement of the secondary bronchi, it is the most simple positive measure of diagnosis at our disposal. Bronchoscopy can most easily be carried out under local anesthesia; although in the highly nervous patient avertin or evipan may be used.

Several important observations can be made by this method: (1) a definite nodular growth may be seen from which a small portion can be removed and submitted to microscopical examination; (2) narrowing due to submucous infiltration by growth or that due to pressure by a tumor outside the bronchus may likewise be determined; and (3) broadening of the carina due to enlarged mediastinal glands below the bifurcation of the trachea can be visualized. In fact, it would be no exaggeration to say that bronchoscopy should be performed on the majority of patients, especially those who are of middle age, who have had hemoptysis and in whom tubercle bacilli cannot be found on examination of the sputum.

Another observation which I think may be of value is that it is almost invariably impossible to perform a lobectomy on any patient in whom the growth can be seen by bronchoscopy, and in these cases the only radical operation that could be considered would entail a total removal of the affected lung.

ARTIFICIAL PNEUMOTHORAX

The introduction of air into the pleural space, when it is not prevented by adhesions, may serve to distinguish tumors of the inner

chest wall and pleura from those arising in the pulmonary tissue and, therefore, may be of considerable value if the question of operation is being considered.

THORACOSCOPY

This method of diagnosis may also add to our knowledge of the conditions present within the pleura, as it may give evidence of secondary involvement of the pleura, a condition which would contraindicate any attempt at radical operation.

PLEURAL EFFUSION

Where pleural effusions are present, Mandlebaum's method of examination may enable a positive diagnosis to be made. This method comprises the withdrawal of a quantity of the fluid, subjecting it to centrifugalization, pouring off the supernatant fluid and hardening the deposit by formalin, after which it is prepared for microscopic section and examination as is the usual solid section. Incidentally, this method may be used for sputum examination in suspected cases. Rarely, portions of growth are expectorated and can be submitted to microscopy.

EXPLORATORY THORACOTOMY

Necessarily, this method should be employed last and particularly in cases in which the diagnosis cannot be arrived at by other methods. By modern methods it entails no greater risk than abdominal exploration. In two patients with suspected malignant disease exploratory thoracotomy disclosed teratomas, one being of enormous size, both of which were successfully removed.

PATHOLOGY

I do not propose to take much time for discussion of the pathology of malignant disease of the lung. It is now well recognized that carcinoma is the predominating lesion and sarcoma relatively rare. In recent years it has been demonstrated beyond doubt that the so-called "oat-celled" growths are carcinomatous and not sarcomatous.

Further, there is a growing opinion that all the carcinomas in the lung arise in the bronchi or bronchioles. In fact, considerable doubt has been cast on the view formerly held that carcinoma arises in the alveolar epithelium.

A point of considerable interest is that the majority of the carcinomas of the lung are of the "squamous-celled" type. Two theories have been put forward to explain this: In the one, it is suggested that metaplasia or rather anaplasia of the columnar cells of the bronchial mucous membrane takes place as a result of irritation and that the carcinomatous changes arise in these squamous cells. A more feasible and attractive theory has been formulated by Fried who is

of opinion that the carcinomatous change takes place primarily in the basal undifferentiated cells of the bronchial mucosa, the result of which accounts for the variation of the types of carcinoma, not only in different individuals, but in different portions of the growth in the same individual.

TREATMENT

Treatment of pulmonary carcinoma for many years consisted in medical measures directed to the alleviation of the predominant symptoms, largely by drugs for the control of pain, and no attempt was made to deal with the lesion itself. Subsequently x-ray treatment was given, and it is generally agreed that the results were more than doubtful. Furthermore, owing to the relative inaccuracy of the diagnosis, especially as regards the site of origin of the mass, whether primary pulmonary or primary mediastinal, further doubt was cast upon the value of x-ray therapy in true pulmonary malignant neoplasms.

No one of experience could doubt the value of deep x-ray therapy, at any rate temporarily, in the treatment of such conditions as mediastinal sarcoma, lymphosarcoma or lymphadenoma. Even in these, however, there is a marked tendency to recurrence, especially in the more malignant types, which often disappear with extraordinary rapidity when first submitted to irradiation.

Some years ago I was taken to task for stating that I had yet to see a patient with a proved carcinoma of the lung not only cured but obviously improved by deep x-ray treatment. However, I must confess that some fifteen months ago a patient of mine submitted to this form of treatment did show a remarkable disappearance of a growth projecting from the upper lobe bronchus and proved by section to be a squamous-celled carcinoma. Multiple secondary deposits, however, were evident in three months, certain of which disappeared on further treatment, but the patient finally succumbed eleven months later to multiple secondary deposits including large numbers of nodules in the subcutaneous tissues. Perhaps, however, the future results of treatment of pulmonary carcinoma by x-ray will disprove the somewhat gloomy views I now hold.

RADIUM

As the majority of these pulmonary carcinomas are of the squamous-celled types, it occurred to me some four years ago that some attempt might be made to submit those patients in whom the growth could be seen in the bronchi by bronchoscopy to the direct effect of gamma radiation.

Some metal containers were, therefore, made for me, which would hold, eight, twelve or sixteen radon seeds. These containers were made in the form of tubes with a lumen to allow secretions beyond the

growth to pass through it while it was in situ. A long thread was affixed to the upper end of the container which was brought out and fixed to the cheek. The original intention was that these should be left in situ for a few hours and then withdrawn. We were rather surprised to find that patients would often retain them without difficulty for periods up to seven days. Subsequently only a small portion of thread was attached to enable the tube to be withdrawn easily by a second bronchoscopy a week after introduction. This small thread allows withdrawal even if the tube passes beyond the growth.

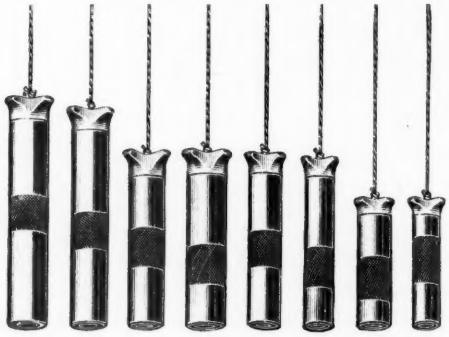

Fig. 1.—Author's radon seed container, Type I.

Fig. 2.—Author's radon seed container, Type II.

These tubes are impacted in the lumen of the bronchus narrowed by the growth, the small flange at the top tending to prevent the tube passing beyond the growth. In some cases where the lumen is completely blocked, it is found by fine bougies and dilated sufficiently to admit the narrowest tube. Subsequently, large sizes can be used. After some years, it was found that though the tubes might be adequate for those growths producing definite narrowing of the lumen, they could not be kept in position for the relatively small earlier growths occupying only a portion of the circumference of the larger

bronchi. Another type was, therefore, devised which would retain itself in any desired position by the gentle pressure of the retaining springs. These are inserted by means of a special introducer and are equally easily removed, the springs being retracted almost into the lumen of the tube.

The seeds are made in 1.5 millicurie strength and the containers hold from 8 to 16 of these. The seeds are surrounded by 0.3 mm. screens of platinum, gold or silver. The former are advisable, as they

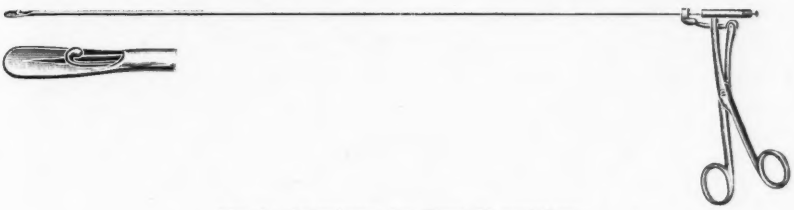

Fig. 3.—Introducer for Type II container.

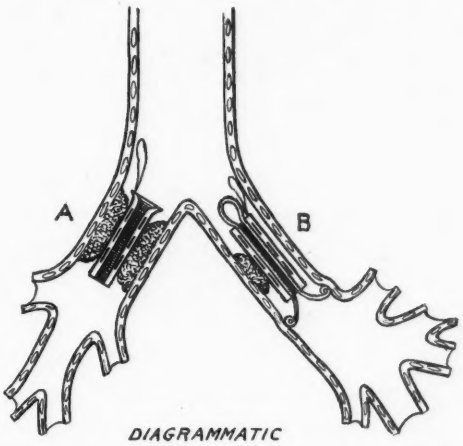

Fig. 4.—Diagrammatic representation of two types of radon seed containers in situ. *A*, showing growth forming stricture; *B*, showing early growth involving portion of wall of main bronchus.

cut off a much larger proportion of the beta rays, which have a cauterizing effect. When using platinum, 99 per cent of the beta rays are cut off; with gold 97.8 per cent, and with silver only 80 per cent. The containers are retained by the patient for seven days, the growth receiving an amount of gamma radiation equivalent to 1,795 milligram hours of radium.

RESULTS

The end-results as regards cure are necessarily poor owing to the late stage at which the diagnosis is made. There have been, however,

some very definite effects. In quite a large proportion of cases it is possible to effect disappearance of the growth in the bronchus. This has been repeatedly seen even when the patient has eventually died of extension of the disease in the lung, and has a definite value of its own. Many of these patients suffer from the effects of retention of the pent-up secretions behind a growth, resulting in high temperatures, wasting, and general malaise.

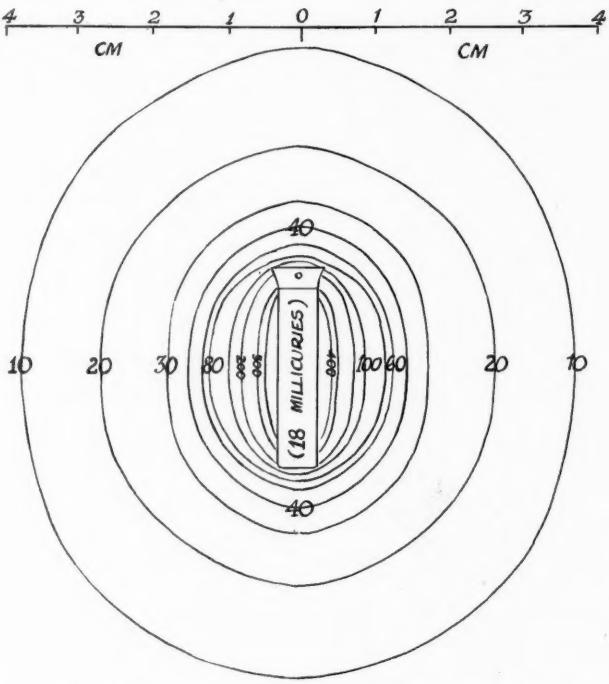

Fig. 5.—Dose contours around radon tube (in r/hours).

Canalization of the bronchus will relieve these secondary conditions, and there is often surprising improvement in every respect. Furthermore, the disappearance of the local growth is a definite indication that, if these patients are seen at an early stage, there is as definite a hope of curing them by irradiation as there is in the early carcinoma of the tongue. In fact, the patient in one of the early cases of carcinoma of the right bronchus who was first treated by this method in 1931 not only is still alive and well but there was no evidence of the growth except for a white scar in the bronchus when examined a few weeks ago; that is three years' freedom from recurrence. Several

other patients are alive from periods of two or three months to over a year. Nevertheless, it cannot be denied that the majority of thirty-two patients submitted to this treatment have died of their growths.

Fig. 6. Fig. 7.

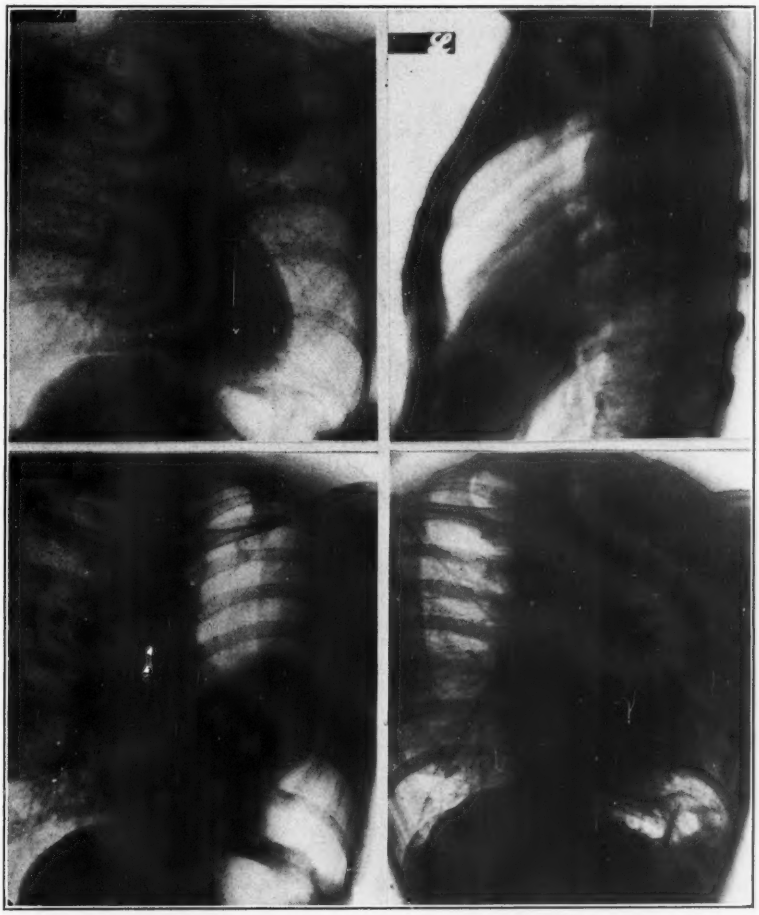

Fig. 8. Fig. 9.

Fig. 6.—Case 1. Secondary deposit in left upper lobe. Local removal of myeloma of fibula twenty-one years before, followed by amputation six years ago.

Fig. 7.—Case 1. A lateral view of same condition as shown in Fig. 6.

Fig. 8.—Case 1. Anteroposterior view in erect posture after pneumothorax. (N.B. Apex has dropped to level of fourth rib anteriorly.)

Fig. 9.—Case 1. X-ray picture taken six and one-half years after subtotal upper left lobectomy.

The obvious lesson to be learned is one regularly preached about all types of carcinoma, that good results from any form of treatment depend upon early diagnosis.

THORACOTOMY AND DIRECT INSERTION OF RADON SEEDS

Open thoracotomy by intercostal incision may be advised if no growth is visible by the bronchoscope. First, it makes the diagnosis certain; second, it gives the patient the chance of radical operation if the growth is operable; and third, it gives an opportunity for the insertion of radon seeds if radical procedures are out of the question. There is no doubt that as experience of pulmonary resection increases we shall find more operable cases. Even elderly patients stand thoracotomy, properly performed, extremely well.

In this series 41 patients were submitted to thoracotomy, the oldest four being respectively sixty-four, sixty-five, sixty-six and sixty-nine years of age, all of whom survived operation not less than twelve months. Of these 41 patients, 14 have been submitted to radical procedures

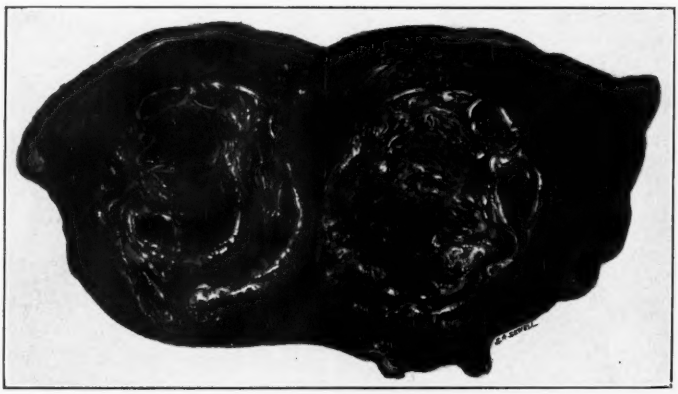

Fig. 10.—Case 1. Major portion of upper left lobe after removal.

and 27 have had radon seeds inserted when radical operation was found impossible. Analyzing the group submitted to thoracotomy and insertion of radon seeds and excluding two patients who died within ten days, one of cerebral hemorrhage and the other of bronchopneumonia, and also excluding patients still alive, the average length of survival is twelve months after operation. This compares very favorably with the average length of life of patients with pulmonary carcinoma who have received no operative treatment, which is stated to be from four to five months after diagnosis has been made. Furthermore, many of these patients have been relatively well and able to resume their occupations for some months before relapse occurs. Others have been relieved of intolerable pain, and in some patients there has been a temporary gain in weight of even as much as 42 pounds. Of these surviving, one patient is alive and symptomless four years after

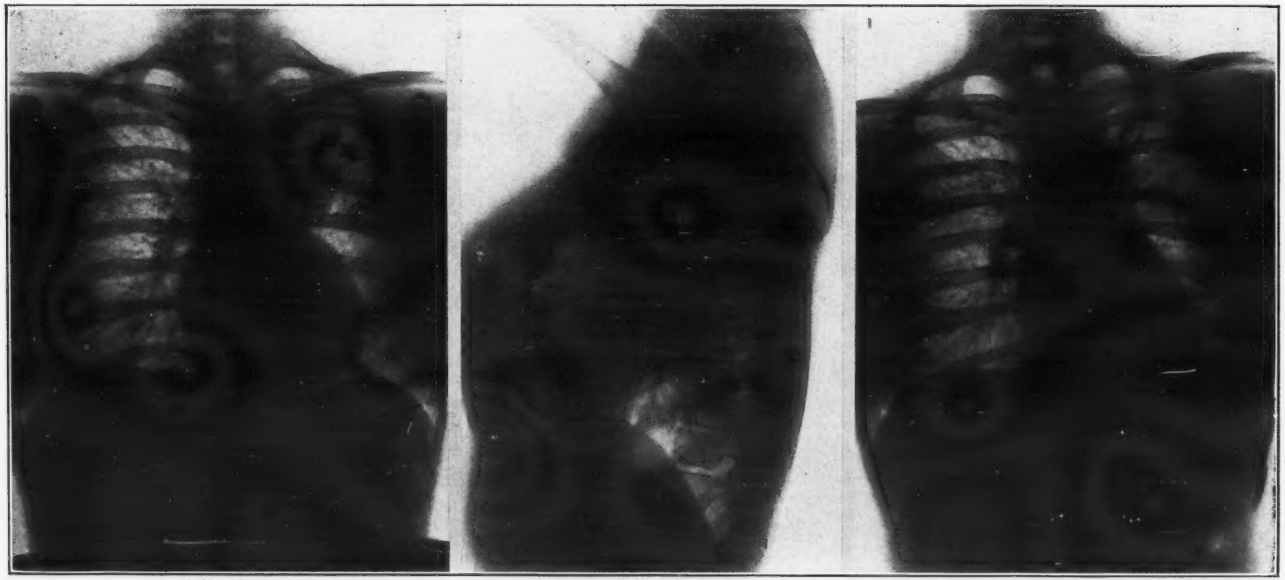

Fig. 11. Fig. 12. Fig. 13.

Fig. 11.—Case 2. Radiogram of columnar-celled carcinoma of left upper lobe, anteroposterior view.
Fig. 12.—Case 2. Lateral view of same condition as shown in Fig. 11.
Fig 13.—Case 2. Eighteen months after operation. (Patient is still alive and well four and one-half years after operation.)

operation, another two years, another twenty months, and two others ten months and six months respectively, although both the latter show evidence of secondary deposits.

Fourteen patients have had their growths removed, including amounts of pulmonary tissue varying from a portion of one lobe to the whole of one lung. One patient (Case 1), a woman with a secondary myelosarcoma, is still alive and well six years and nine months after subtotal resection of the left upper lobe. A second patient (Case 3), a woman, is alive and well five and one-half years after removal of the right lower lobe for a large endothelioma. Another woman has survived partial lobectomy for a columnar-celled carcinoma in the left upper lobe for just under four and one-half years (Case 2). A fourth

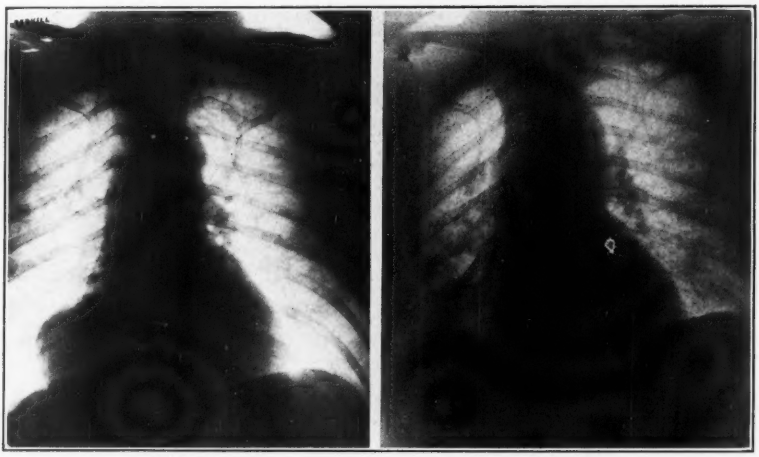

Fig. 14. Fig. 15.

Fig. 14.—Case 3. Endothelioma of right lower lobe.
Fig. 15.—Case 3. Almost two years after right lower lobectomy. (Patient still alive and well five and one-half years after operation.)

patient, a man, is alive and symptomless eleven months after lower left lobectomy for carcinoma. A fifth patient (Case 4), is convalescent following lobectomy six weeks ago for endothelioma of the lower left lobe. Three patients succumbed within ten days of operation from: (1) delayed cardiac failure—this patient left the operating table with a pulse of 90 and good blood pressure after middle lobectomy for carcinoma; (2) hemorrhage—from a divided intercostal vessel in suturing the chest wall following lower lobectomy and removal of a portion of the diaphragm; and (3) secondary infection. Another died six weeks after upper left lobectomy from severe infection in a residual apical empyema cavity. Three other patients have died of recurrence or secondary deposits at intervals of from four to twenty months after

operation. Two of these died of mediastinal involvement, one in four months and one in twenty months. The other died of a secondary

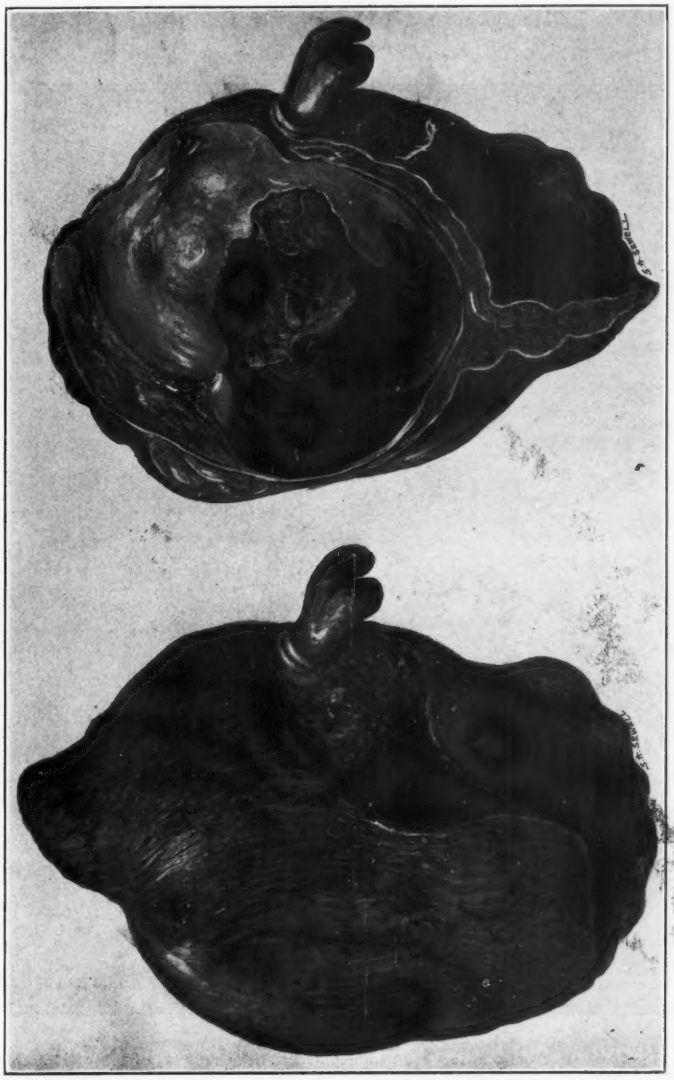

Fig. 16.—Case 3. Lobectomy, lower right lobe. Note that bronchus has retracted after removal of clamp allowing growth to project.

cerebral deposit six months after removal of the left upper lobe with a squamous-celled carcinoma, in addition to which he had a similar type of carcinoma of the palate removed by diathermy three weeks after lobectomy.

The last two were patients requiring total pneumonectomy, both of whom died. The first of these who had a carcinoma the size of a large orange in the right lung was subjected to a thoracoplasty in addition to the pneumonectomy. He got through the postoperative

Fig. 17. Fig. 18.

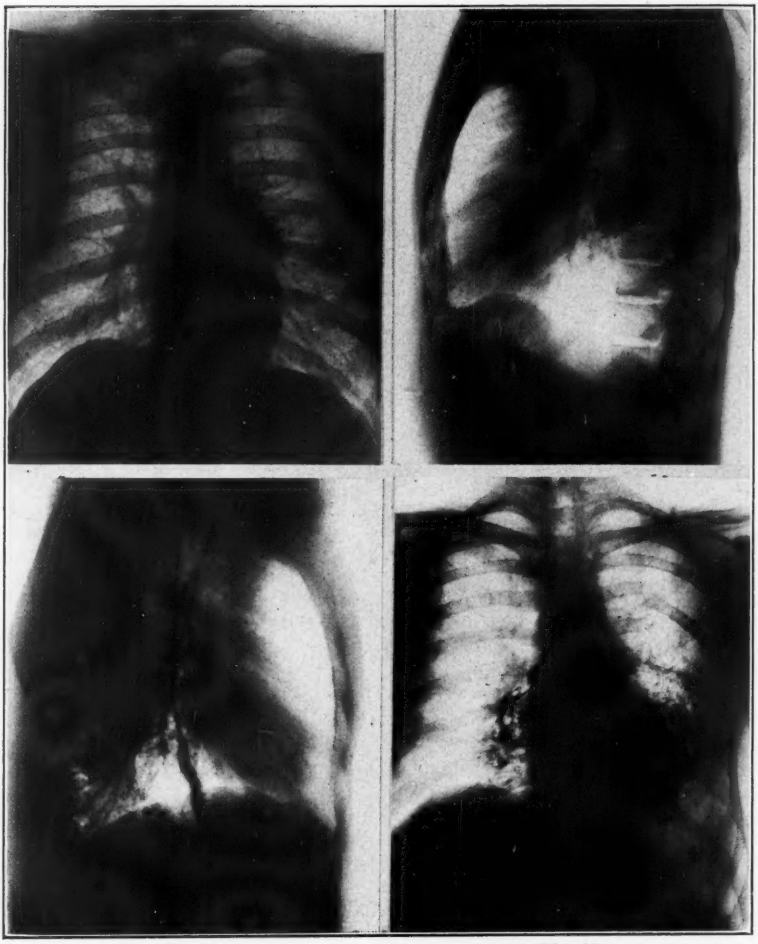

Fig. 19. Fig. 20.

Fig. 17.—Case 4. Tumor in left lung immediately above and overlapping shadow of left edge of heart.

Fig. 18.—Case 4. A lateral view of same condition as shown in Fig. 17, showing the tumor immediately behind and below pulmonary hilum.

Fig. 19.—Case 4. A lateral bronchogram showing first posterior bronchus to lower lobe blocked at junction with tumor.

Fig. 20.—Case 4. Bronchogram ten weeks after lower lobectomy for endothelioma. Upper lobe expanded to fill major portion of left chest. Patient alive and well three months after operation.

period very comfortably. A bronchial fistula became obvious on the tenth day but did not cause any anxiety; however, on the fifteenth day his pulse began to fail in volume and to increase in rate, and death occurred on the evening of the sixteenth day. Autopsy revealed a well-drained empyema cavity and a suppurative pericarditis. The only evidence of dissemination was a small secondary nodule in the liver.

The second patient, who also was submitted to a total right pneumonectomy for a columnar-celled carcinoma about the size of a small fist close to the hilum, survived operation only three days, was

Fig. 21.—Case 4. Lower left lobe after removal for growth.

satisfactory on the day following operation, but on the second night showed evidence of secondary cardiac failure, and died the third night. Autopsy on this case revealed myocarditis and no other cause for death.

Both of these patients were operated on from a posterior incision which offers definite difficulties in the approach to the hilum if the growth is at all bulky. It appears to me that in such cases an anterior approach to the hilum and control of the blood supply might be advisable.

This is a point on which I am looking forward to hearing the views of other surgeons who have used this approach.

Where there is a carcinoma obstructing the bronchus, the lobe is usually contracted and airless and the posterior approach probably sufficient.

There are several points worthy of study, however, in regard to total pneumonectomy. Is thoracoplasty necessary either as a preliminary, at the time of operation, or subsequently? The chest walls of older patients do not collapse well owing to calcification of the costal cartilages; and if thoracoplasty is required, it would appear to be necessary to carry out a very extensive costal resection to obtain an effective collapse. We are brought back again to the problem of the permanent closure of the bronchus, when no tissue is left in the hemithorax by which it can be covered.

In regard to pneumonectomy, it is most impressive how little shock appears to be associated with this apparently formidable procedure.

In conclusion, it would appear that by one means of treatment or another we can now offer to a fair proportion of patients suffering from malignant pulmonary disease definite relief and prolongation of life and to a smaller proportion a chance of cure.

BRONCHIOGENIC CARCINOMA: A CLASSIFICATION IN RELATION TO TREATMENT AND PROGNOSIS*

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NATHAN A. WOMACK, M.D., ST. LOUIS, MO.

ONE of the major problems connected with the subject of primary bronchiogenic carcinoma is concerned with the question of whether surgical removal or radiotherapy is the more effective method of treatment. Enough examples of radical surgical removal are now on record to make of this a feasible procedure and one which would seem to offer some assurance of freedom from recurrence. On the other hand, claims have been made by some radiotherapists of results which challenge those of the surgeon. Before unqualified acceptance of those claims, however, it should be emphasized that it is only in the exceptional case that the claim has been made and the infrequency of the alleged results must necessarily cast some suspicion on the accuracy of the diagnosis. It is possible, however, that certain cases may be shown to be more susceptible to radiotherapy than others. From the present study it will be seen that marked differences in the morphology and malignancy exist depending somewhat on the site of origin of the tumor. Adequate information is not available to include in this paper any satisfactory conclusions about the comparative radiosensitivity of the different kinds of tumors discussed here, but it is hoped that future reports of the use of radiotherapy by others as well as ourselves will give more detailed information regarding the structure and the location of the tumor than is usually given in such reports. It is felt that this information may be the beginning of a kind which, when enlarged by the experiences of others, may have some importance in arriving at a decision in regard to the treatment of a particular case. In addition certain pathological and experimental observations have been correlated to clinical findings. We shall not attempt a critical review of the subject as there have been several excellent studies of that type. We shall, however, attempt to classify primary cancers of the lung from the standpoint both of morphology and of prognosis.

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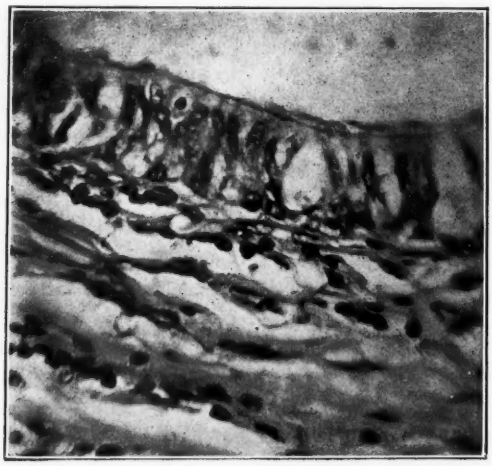
In the absence of Dr. Tuttle and Dr. Womack this paper was presented by Dr. Evarts A. Graham. In discussion the references to Dr. Graham's paper in general refer to this paper by Dr. Tuttle and Dr. Womack.

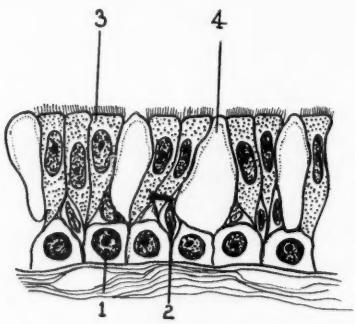
†National Research Council Fellow.

ANATOMY

Most, if not all, primary carcinomas of the lung arise from bronchial epithelium. This epithelium is a direct continuation of that of the trachea and varies in arrangement as the bronchus decreases in size. The major bronchi near the tracheal bifurcation are lined by stratified epithelium. (Fig. 1 *A* and *B*.) Resting on a basement membrane there



A.



B.

Fig. 1.—*A*, Photomicrograph of epithelium of major bronchus.
B, Diagrammatic sketch of bronchial epithelium showing (1) basal cell, (2) indifferent cell, (3) ciliated cell, (4) goblet cell. All these cells may be identified in *A*.

is a layer of round or polygonal cells basal in type and comparable to the basal cells of the epidermis. These probably represent the germinal cells, as it is from this layer that growth can be observed following experimental injury in animals. Extending up toward the lumen of the bronchus are spindle cells of three types, ciliated cells, goblet cells, and

a third or indifferent cell, the former two of which reach the bronchial lumen. This latter type probably has the power to differentiate into either the ciliated or the goblet structures. As the bronchus decreases in size the epithelium thins out and also becomes less spindle shaped, until by the time the ductus alveolaris is reached it is cuboidal

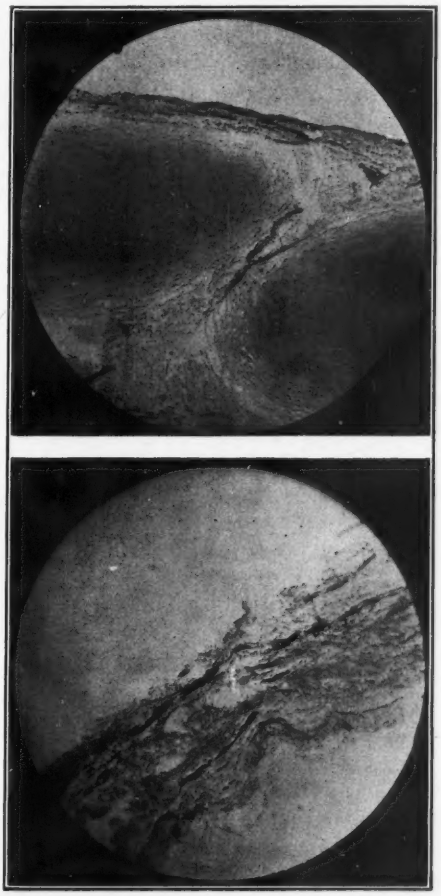


Fig. 2.—*A*, Photomicrograph of bronchus of a dog after the injection of India ink beneath the mucous membranes. The ink particles can be seen in the submucosal plexus of lymphatics extending outward between two cartilaginous rings to the adventitial plexus.

B, Section taken from area of bronchus of dog in which cartilaginous rings are absent, showing infiltration of adventitial lymphatics.

or low cuboidal. Whether the lining of the alveolus is a continuation of these cells is still a disputed point and need not concern us here. It is of importance, however, to recall that the mucous glands in the wall of the bronchi apparently have their origin from the bronchial

epithelium. Their ducts are largely lined by ciliated cells continuous with those of the lumen of the bronchus, and the mucous glands are composed of cells similar to goblet cells. This genesis of the mucous glands is important because it simplifies the classification of bronchiogenic carcinoma. Since all the structures have the same origin, it is unnecessary to consider a separate classification of mucous gland cancer.

Directly outside the submucosa the bronchial cartilages are arranged. These are U-shaped in the major tubes, but as the bronchus becomes smaller the cartilages become smaller, multiple, and finally disappear. It is probable that they serve an additional function in the presence of tumors of the major bronchi by offering a certain amount of ob-

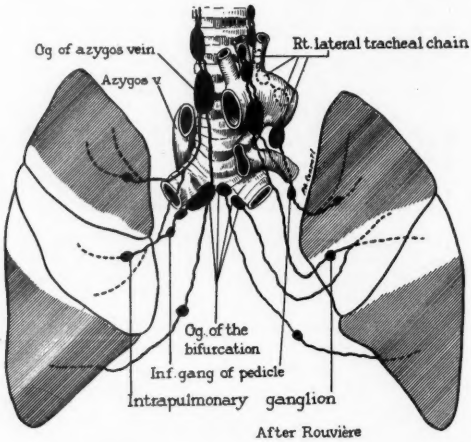


Fig. 3.—Diagrammatic sketch showing regional nodes draining bronchial lymphatics. The upper shaded areas drain only into the lateral tracheal chains. The middle white areas drain into both the lateral tracheal chains and the glands at the bifurcation. The lower shaded areas drain only into the glands at the bifurcation.

struction to extension, an obstruction that becomes less as the cartilages become smaller and fragmented.

Any consideration of the spread of cancer of the lung must appreciate the lymphatic system of this region. This is a complicated system and in its detail not all observers are in accord. However, there are certain features fairly well understood, and these are of clinical importance.

Within the lung there are two systems of lymph vessels, the deep and the superficial lymphatic plexuses. The deep vessels follow the bronchi and blood vessels toward the periphery of the lung and end in the ductus alveolaris. Apparently there are no lymph channels in the walls of the alveoli. The superficial vessels extend near the sur-

face of the lung immediately beneath the pleura where they connect by short branches with the vessels of the deeper system. Because of the presence of valves in the superficial system, lymph flow is possible only toward the hilus, while in the deep set in which there are no such valves the flow may take place in either direction. Within the short anastomosing branches between the two systems, valves are present which, while they allow the egress of lymph from the deep to the subpleural plexus, prohibit flow from the latter to the former.

Immediately beneath the mucosa of the bronchi there is a rich plexus of lymphatics which may be easily demonstrated by India ink injections in the fresh specimen. (Fig. 2 *A* and *B*.) Vessels from this plexus extend out between the cartilage rings to unite with another plexus of vessels in the adventitia of the bronchus. As the bronchi become smaller these two plexuses gradually merge. Channels from the adventitial plexus extend toward the major bronchi to the interlobar nodes, the nodes at the tracheal bifurcation (intertracheobronchial nodes) and the lateral tracheal nodes. The exact pathway of drainage depends on the location in the lung. This is represented schematically in Fig. 3, as has been demonstrated by Rouviere.[1] We have been able to verify these findings by the injection of carmine suspensions in various portions of the lungs. It is important that these pathways be recognized. Any operation for carcinoma to be complete must remove the regional lymphatics. Therefore any lobectomy or pneumectomy for carcinoma of the bronchus to be adequate must carry with it the excision of the proper lymphatics.

REACTION OF BRONCHIAL EPITHELIUM TO INJURY

When a small defect is made in the bronchial epithelium, repair takes place by an outgrowth of the basal cells. At first these new cells are low cuboidal or squamous but later take on a columnar or spindle appearance as they become older and more stratified. This faculty of the bronchial epithelium to change its morphologic characteristics is one of its most prominent features. When adult bronchial epithelium is subjected to long standing chronic inflammation as in bronchiectasis, hyperplasia may occur. This hyperplasia may take the form of a metaplasia in which the epithelium becomes stratified squamous in type resembling epidermis. (Fig. 4 *A*.) Occasionally the hyperplasia may involve chiefly the goblet cells, and in these areas it is often difficult to demonstrate ciliated cells for a considerable distance. (Fig. 4 *B*.) We have observed both in bronchiectasis. The idea that this change represents the first stage in the formation of carcinoma has been suggested by others, and such a conception seems to be a rational one. Unfortunately in our experience and in that of others statistical studies offer little support of this idea. In 76 cases of primary bronchiectasis in patients of the cancer age, seen in the Chest Service of

the Barnes Hospital, there has been observed only one patient who subsequently developed bronchiogenic carcinoma. This experience is not unique. We cannot help but feel that many of the reported cases of cancer occurring in the walls of bronchiectatic cavities are

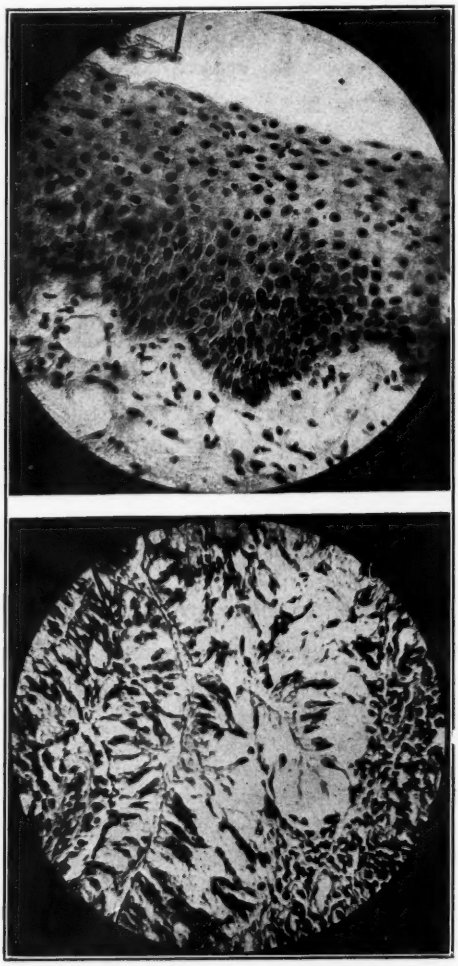


Fig. 4.—*A*, Extreme squamous metaplasia of bronchial epithelium in a patient with bronchiectasis.
B, Hyperplasia of goblet cells of bronchial epithelium in a patient with bronchiectasis.

actually primary carcinoma with secondary bronchiectasis. Likewise in only one of our cases of carcinoma have we been able to obtain a previous history of active pulmonary tuberculosis. A comparison

with lupus of the face which is occasionally followed by squamous cancer is not an accurate one. The scarring and nutritional changes seen in an old lupus are not usually present in the submucosa of the bronchus in pulmonary tuberculosis. Accordingly we are inclined to consider these hyperplastic and metaplastic changes so often seen in chronic inflammatory lesions of the lung as a protective mechanism rather than a precancerous change. And the apparent ease with which bronchial epithelium may become stratified squamous in type probably explains the frequency with which this sort of epithelium is encountered in bronchiogenic carcinoma.

PATHOLOGY

At the Chest Service of the Barnes Hospital the diagnosis of primary cancer of the lung has been made in approximately 150 instances in the last nineteen years. In some of these cases for various reasons a biopsy was not done or an autopsy was not obtained. Many of these cases were undoubtedly carcinoma. However, this study is based on only those patients who were studied clinically and from whom tissue was obtained either by biopsy or at autopsy. There is a total of 60 such cases. Although all 60 cases have been used in this study, for various reasons 44 cases are the largest number to appear in any one particular table.

The gross appearance of a lung involved by primary carcinoma varies considerably. For this reason numerous classifications have appeared in the literature. Most of these are descriptive. In the earliest stages one sees a piling up of the mucous membrane with gradual extension along the mucosa and out into the lumen of the bronchus. This occurs before the adventitial lymphatics have been invaded. We have seen four such cases. In three of them the tumor arose in the lower lobe bronchus immediately below its division from the main bronchus and had grown along the mucosa entering the middle or upper lobe bronchus. In the fourth case the extension had been into the middle lobe bronchus from the upper lobe bronchus. Such a process may remain localized in the bronchial wall for some time. In one of the above mentioned cases there was clinical evidence that the tumor had been present for three years. However, once the wall has been penetrated and the lymphatics or blood vessels invaded, extension is much more rapid. The picture presented becomes one of a fan-shaped grayish mass infiltrating out into the lung parenchyma with various stages of necrosis and abscess formation. Not so commonly one sees the tumor as a diffuse growth involving the entire lobe or even a whole lung giving a picture not unlike that seen in the gray hepatization of pneumonia. Also rarely the tumor may be found as single or multiple nodules in the parenchyma of the lung with no apparent connection with the larger bronchi.

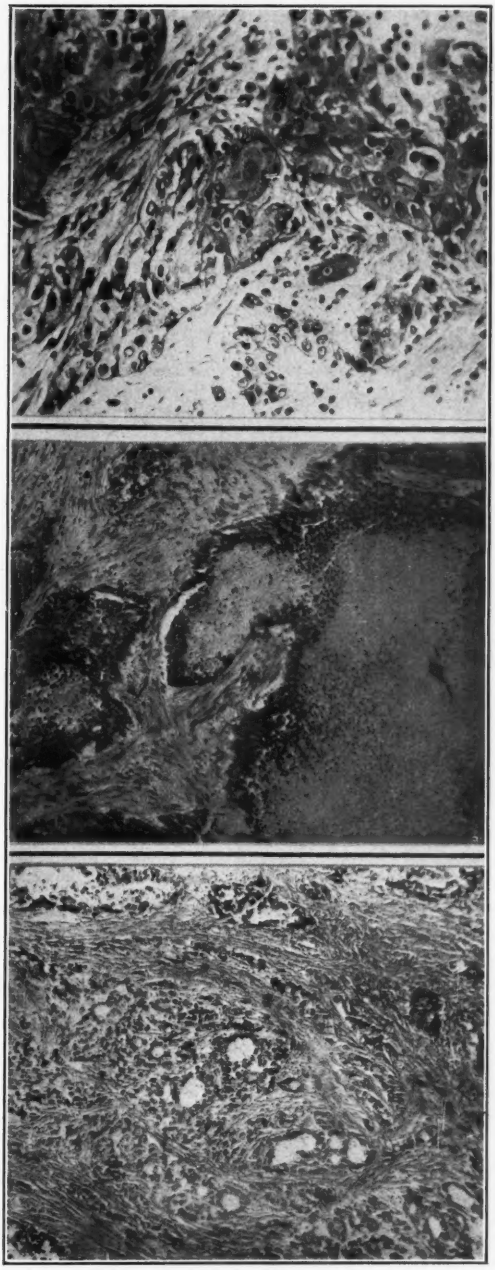
Other classifications have been made according to histogenesis, namely, tumors arising from (A) bronchial epithelium, (B) bronchial mucous glands, and (C) alveolar epithelium. The first group is self-evident. The second group deserves some attention. It is supposedly composed of those cancers arising in the bronchi and not associated with ulceration but limited to the bronchial wall and causing stenosis. The histologic picture is often that of adenocarcinoma resembling mucous glands. While we have had several tumors suggestive of this group, none of them have been clear-cut. Since the mucous glands have the same origin as bronchial epithelium, we have seen no reason for making a separate classification for this group on the basis of genesis. As we have seen, all the epithelial elements of the lung arise from the same primitive bronchial epithelium; all primary cancers of the lung may therefore be considered genetically as bronchiogenic carcinoma. While any of the above classifications may be used for descriptive purposes, we have found them to be of less clinical value than the statement as to the location of the tumor. As we shall later show it is of considerable clinical importance to determine whether the tumor is located in a major bronchus or whether it is peripheral to a major bronchus. Moreover, this is a classification that usually can be made during life either by x-ray visualization of the bronchus following lipiodol injection or by direct visualization by a competent bronchoscopist. We have, therefore, classified these tumors as bronchiogenic carcinomas (A) arising in a major bronchus and (B) arising in a minor bronchus or the lung parenchyma. In our series 23 cases were in Group A, and 21 cases were in Group B.

Secondary changes in the lung distal to the tumor often distort the picture. Perhaps the most common is that of atelectasis. This frequently involves an entire lobe and is erroneously interpreted at times in the x-ray film as the tumor. Atelectasis is often an early finding, and we have seen it on several occasions associated with a small operable tumor that had rapidly occluded the lumen of the bronchus. Associated with the atelectasis are often encountered abscess formation and bronchiectasis. So common is this that pulmonary suppuration of unknown origin occurring after the age of forty should always be regarded with suspicion. Even at autopsy the abscess formation may be so prominent that the carcinoma may be overlooked. It seems probable that this possibility may be one explanation of the fact that

Fig. 5.—*A*, Small group of malignant epithelial cells removed at bronchoscopy showing attempt at formation of squamous epithelium.

B, Massive necrosis of bronchiogenic carcinoma giving gross picture of bronchiectasis. It is this type of lesions that has probably been erroneously considered in the past as primary bronchiectasis with subsequent carcinomatous formation.

C, Glandular type of carcinoma infiltrating the bronchial wall and tending to form mucous glands. In our opinion there is nothing to be gained by making a special classification of this type of tumor.



A.

B.

C.

Fig. 5.—(See opposite page for legend.)

carcinoma of the bronchus was formerly regarded as much less common than at the present time.

Pleural involvement, encroachment on the major vessels with obstructive symptoms, involvement of the upper mediastinal and cervical nodes are all late manifestations. The picture seen in such cases is usually an evident one and will not be considered in detail here.

The microscopic picture seen in bronchiogenic carcinoma is most varied. With the exception of perhaps the thyroid gland there is hardly a structure in the body that presents more pleomorphism. (Fig. 5.) This has led to considerable confusion in an effort to obtain a cytologic classification. Numerous descriptive terms have appeared as adenoid, spindle cell, squamous cell, pavement cell, round cell, oat cell, alveolar, papillary, and mucous gland carcinoma. It must be remembered that these terms are solely descriptive of the types of

Fig. 6.—Photomicrograph showing evidence of pleomorphism of bronchiogenic carcinoma. In this section two different phases of tumor growth may be seen. (Courtesy of Dr. S. H. Gray.)

tumor formation that may at times be encountered. They offer little aid as to the genesis of the tumor and even in describing the tumor such terms are inaccurate. Figs. 6, 7 *A* and *B*, show that entirely different phases of growth can exist in the same tumor. Thus in our opinion one is never justified in speaking of mucous gland carcinoma or alveolar cell carcinoma, etc., merely because, in certain portions of the tumor, cells or groups of cells tend to form mucous glands or alveoli.

A classification of bronchiogenic carcinoma based on degree of differentiation will be discussed later in this paper.

METASTASES

Carcinoma of the lung has many peculiarities when it is considered from the standpoint of its metastases. Often a large pulmonary tumor will remain localized in the lung for a relatively long period of time.

At other times metastases may occur very early in the course of the disease. Frequently the first symptoms that are noticed are from such extensions. This is especially true of secondary lesions in the brain, where we have seen seven such instances. Ryerson and Hirsch[2] have reported four cases of skeletal metastases that were first regarded as primary bone sarcoma. Such lesions are obviously those

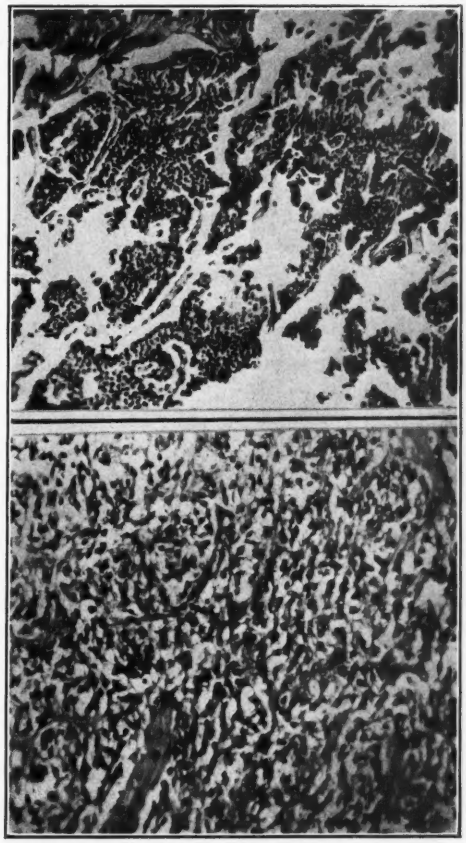


Fig. 7.—Two views of the same tumor shown in Fig. 6, taken from different regions. *A*, shows a polygonal pavement type of epithelium while *B* shows an abortive effort on the part of the cells to form mucus.

following extension into blood vessels, and in our experience this is seen more commonly in tumors arising in the periphery of the lung than in those connected with the major bronchi. Fig. 8 shows such a mechanism. Such a phenomenon could be explained by the increased vascularity of lung tissue compared to that of the bronchus, thinness

of the vessel walls in the lungs, and increased mobility of the lung with associated intravascular pressure changes.

Extension by way of the lymphatics generally takes place through the pathways that have been previously outlined. An experimental study of these pathways was undertaken. One cubic centimeter of a carmine suspension was injected beneath the pleura of the lower right lobe of one dog and a similar amount of the same suspension injected in the wall of the lower right major bronchus at a point just before it entered the lung in another dog of approximately the same age. At the end of five days the animals were sacrificed. There was no infection. A striking fact was noticed. The animal that had received the injection in the periphery of the lung had intertracheobronchial lymph nodes brilliantly colored with carmine. The animal that had received the carmine in the wall of the major bronchus to the lobe had only a trace of carmine in the intertracheobronchial nodes. The experiment was repeated in six sets of animals with injections of the various lobes and their concomitant bronchi. The results were consistent. From this experiment we felt justified in concluding that particulate matter from the periphery of the lung was carried to the regional lymph nodes much more rapidly than from the wall of a major bronchus. We were next concerned as to whether carcinoma cells would behave in the same manner, and a statistical study was carried out to determine this point. We found that generally cancer arising in the smaller bronchi and periphery of the lungs pursued a much more rapidly fatal course than a cancer arising in a major bronchus. This will be discussed in more detail in considering the prognosis of the disease.

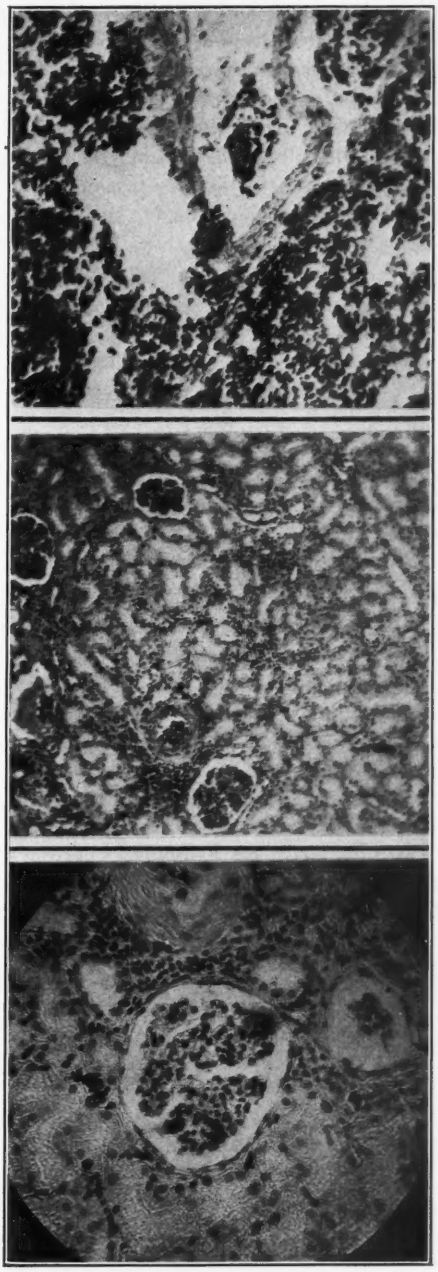
The site of distant metastases is an interesting feature of this disease. Thirty of our cases had complete necropsies, and the sites of the metastases seen most frequently are listed in Table I. Because of the relatively small number of cases these figures must be taken as suggestive rather than conclusive. One would expect the brain to be frequently involved, and it was in 23.3 per cent of our cases. The common occurrence of adrenal gland involvement is more difficult to explain. We noticed it in 33.3 per cent of our autopsies. Two of our patients had been erroneously diagnosed as having hypernephromas. In a similar study Dosquet[3] finds the central nervous system involved in 31.4 per cent of the cases and the adrenal glands in 21.8 per cent. He makes the interesting comparison in metastases from carcinoma

Fig. 8.—Photomicrographs of metastasis by way of blood stream.

A, Bronchiogenic carcinoma invading the wall of a pulmonary artery. A group of carcinoma cells may be seen in the lumen of the vessels.

B, Section taken through the kidney of the same patient showing a small artery and glomeruli containing tumor cells.

C, Higher magnification of one of the glomeruli seen in *B*, showing malignant emboli.



A.

B.

C.

Fig. 8.—(See opposite page for legend.)

primary in other regions with and without pulmonary involvement where he found the central nervous system affected in a total of 2.5 per cent of the cases and the adrenals in a total of 4.5 per cent. In our experience when single lesions are found in the brain, adrenals and lung, the primary lesion generally is in the lung. Multiple lesions in the adrenals make this almost a certainty. Attention is also directed to the large number of metastases to the spleen and the pancreas. We have no adequate explanation for this.

TABLE I

FREQUENCY OF METASTASIS IN VARIOUS ORGANS; A STUDY OF 30 CASES

ORGAN	NO. OF CASES	PERCENTAGE
Liver	13	43.3
Adrenal	10	33.3
Brain	7	23.3
Kidney	8	26.6
Lung	7	23.3
Pancreas	4	13.3
Spleen	3	10.0
Bone	2	6.6
Ovary	1	3.3
Intestine	1	3.3
Skin	1	3.3

Occasionally the lymphatics of the pleura are involved and give the gross appearance of a network of white streaks which have been graphically described as carcinomatous lymphangitis. This type of extension is generally associated with pleural effusion and can be conceivably considered as the mechanism of spread of that type of carcinoma often spoken of in the past as endothelioma of the pleura.

DIAGNOSIS

As a rule, certainty in the diagnosis of a malignant disease is never obtained until the tumor cells are examined microscopically. When this principle is applied to bronchiogenic carcinoma, obvious difficulties are encountered. Biopsy here is not an innocuous procedure. Therefore, since the majority of these tumors are ulcerating into the bronchial lumen, we ran a series of careful sputum examinations. The patient was asked to cough directly into fixing fluid, and the coagulum was blocked and sectioned. It was extremely difficult to demonstrate malignant cells. Occasionally necrotic masses in which the skeleton of the cells could be seen were found. This was generally in those patients who were in a far-advanced stage of the disease, and little valuable information was obtained. The rapid autolysis of the tumor cells in purulent sputum probably renders this method of examination of little practical value.

Another method of direct examination of the tumor tissue is that of fixing and sectioning cells from centrifuged pleural fluid (Mandelbaum[4] and Goldman[5]). When a diagnosis is made by this method, the tumor

has extended past the point of hopeful therapy. In the diagnosis of cancer any method that requires metastases before it can be utilized may as well be discarded so far as the welfare of the patient is concerned. Its value is academic except on those occasions where it may be of service in determining the type of palliation to be used, or in differentiating types of pleural effusion.

In our opinion at the present time the most valuable and rational way of obtaining a biopsy specimen is by the use of a bronchoscope. In the hands of an expert considerable information can be obtained by this method of examination. We feel that this procedure should be used not only to verify a diagnosis but actually to make a diagnosis in suspicious lesions. It is astonishing and depressing how seldom patients with spontaneous atelectasis and spontaneous bronchiectasis are examined bronchoscopically.

PROGNOSIS

The life expectancy of a patient with bronchiogenic carcinoma is a variable factor. One patient in this series died within two months after the onset of symptoms. Two lived for five years. From the

TABLE II

A COMPARISON OF DURATION OF LIFE WITH LOCATION OF THE PRIMARY TUMOR

PATIENT	TUMOR IN MAJOR BRONCHUS	PATIENT	TUMOR IN PERIPHERY OF LUNG
J. B.	36 months	E. B.	6 months
C. B.	12 months	C. B.	33 months
G. B.	18 months	M. D.	6 months
J. B.	23 months	H. D.	10 months
E. B.	46 months	E. D.	3 months
L. D.	14 months	E. H.	9 months
D. D.	10 months	L. H.	10 months
H. D.	24 months	A. K.	6 months
H. K.	60 months	J. M.	6 months
E. M.	12 months	T. M.	8 months
R. M.	4 months	T. M.	14 months
J. M.	30 months	A. N.	5½ months
T. M.	36 months	H. P.	2 months
J. N.	6 months	N. S.	4 months
C. N.	54 months	C. T.	4 months
D. N.	13 months	G. T.	4 months
J. O.	30 months	T. W.	12 months
A. O.	13 months	T. W.	4 months
F. O.	60 months	J. W.	6 months
F. P.	11 months	J. W.	10 months
J. R.	24 months	A. B.	2½ months
J. S.	36 months		
E. S.	36 months	21 cases	155 months
23 cases	607 months		
Average duration 26.3 months		Average duration 7.3 months	

standpoint of the clinician it would be an important aid in treatment to be able to determine to a certain extent the rapidity of progress of this disease. At the present time there is a growing tendency to

be less radical surgically in rapidly malignant lesions, for too often the results are unsatisfactory. On the other hand, the radical extirpation of more slowly growing carcinomas has given results that justify a continuation of the procedure. There is no reason why this principle should not apply to bronchiogenic carcinoma. To select more accurately such cases we have studied our data from two aspects.

The first of these is the grading of the tumors by their morphologic picture. Microscopically a tumor tends to differentiate into cells similar to those from which it arises. The degree of differentiation obtained may be to a large extent dependent upon its rate of growth, i.e., the more rapid the growth the more undifferentiated the cell type. This principle, however, is subject to modification by several factors. One of these factors in bronchiogenic carcinoma is probably the part of the bronchus in which the tumor arises. A carcinoma arising in a bronchiole or a ductus alveolaris where the normal cells are low columnar or cuboidal will as a rule not commonly be of the ciliated or squamous type. A prototype of such a condition is found in squamous carcinoma of the tonsil where keratinization is not so common as in squamous carcinoma of the skin. Thus a poorly differentiated carcinoma of a large bronchus may resemble to a certain extent a rather well differentiated growth beginning in a smaller bronchus more nearly at the periphery of the lung.

In tumors in other parts of the body and in tumors that show much less pleomorphism it has been our opinion that any effort to make a prognosis or to dictate the type of therapy for the patient by the examination of one section of a small bit of tissue obtained at biopsy, is at times an inaccurate procedure. In bronchiogenic carcinoma this inaccuracy must be magnified many times.

With the above facts in mind we have made a cytologic classification on the basis of differentiation, examining several portions of the tumor whenever possible. Under Grade I we grouped those tumors which for the most part tended to resemble adult ciliated cells, goblet cells, or which formed definite squamous epithelium (Fig. 9*A*). Under Grade II we grouped those tumors that for the most part showed a tendency toward differentiation but the cells of which were not quite so mature (Fig. 9*B*). Grade III was made up of cells that to a large extent resembled those of the basal epithelial layer. In this group was placed the so-called round cell carcinoma (Fig. 9*C*).

In Table III it can be seen that if the duration of the disease be measured by the number of months that elapsed from the onset of symptoms to the time of death, Grade I lived for an average of 22.6 months, Grade II for 16 months, and Grade III for 12.8 months or a bit over half as long as the better differentiated lesions. However, let us examine Table V in which a comparison of the grade of the tumor is made with the site of origin. Here it can be seen that the

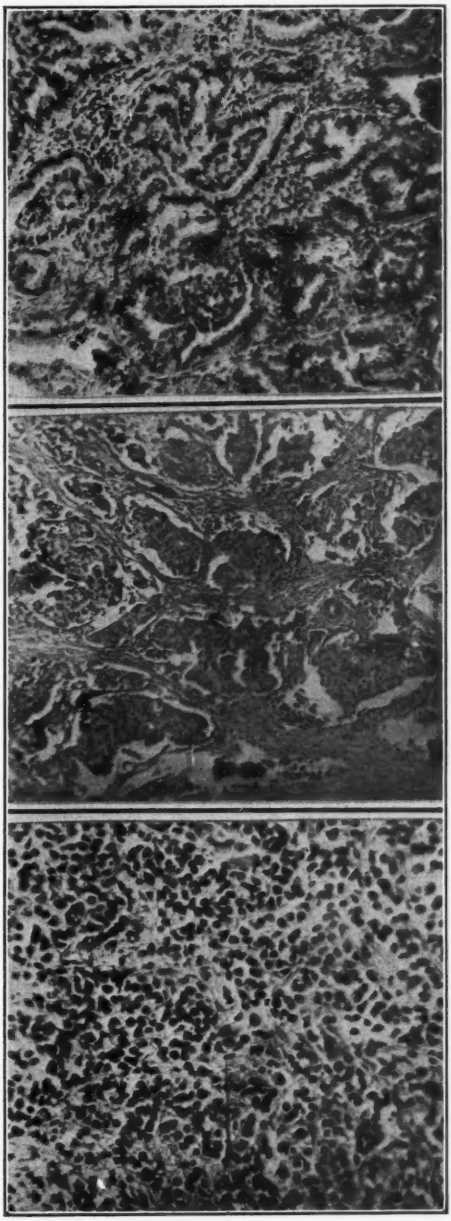


Fig. 9.—Representative degrees of differentiation in bronchiogenic carcinoma. *A*, Grade I. Well-differentiated cells showing an attempt at bronchus formation.

B, Grade II. Polygonal carcinoma cells arranged in pavement formation showing considerably less differentiation than in *A*.

C, Grade III. So-called round-celled carcinoma resembling to a certain extent the basal layer of cells in normal epithelium.

Grade I types are approximately twice as common in the major bronchi as in the minor bronchi, and Grade III types are approximately twice as common in the minor bronchi as in the major bronchi. Furthermore, it will be seen in Table IV that there is only one instance of Grade III and one of Grade II carcinomas in the nine cases in which tumor tissue could be removed by means of the bronchoscope. The rest were composed of the well-differentiated cells of Grade I.

TABLE III

THE RELATIONSHIP OF GRADE OF TUMOR TO DURATION OF LIFE

PATIENT	TYPE I	PATIENT	TYPE II	PATIENT	TYPE III
J. B.	36	C. B.	12	C. B.	33
G. B.	18	M. D.	9	G. K.	6
J. B.	23	D. D.	10	H. K.	60
E. B.	6	E. D.	3	T. M.	8
C. B.	46	J. M.	6	R. M.	4
L. D.	14	J. M.	30	T. M.	14
H. D.	24	D. M.	13	F. P.	11
E. H.	9	A. N.	5	C. T.	4
J. M.	36	F. O.	60	S. T.	4
J. M.	6	J. R.	24	J. W.	6
C. M.	54	N. S.	4	G. P.	2
J. O.	30	F. Z.	2	J. A.	2
A. O.	13	E. S.	36		
H. P.	2	C. H.	1	12	154
14	317	14	215		
Average 22.6 months		Average 16 months		Average 12.8 months	

TABLE IV

THE RELATIONSHIP OF VISUALIZATION OF THE TUMOR AT BRONCHOSCOPY TO THE DURATION OF LIFE

TUMOR VISUALIZED			TUMOR NOT VISUALIZED		
PATIENT	DURATION	GRADE	PATIENT	DURATION	GRADE
J. B.	36	III	C. B.	33	III
J. B.	23	III	E. D.	3	II
C. B.	46	III	J. M.	6	II
J. G.	15+	III	T. M.	14	III
H. K.	60	III	S. R.	18	–
C. H.	54	III	T. W.	12	–
J. O.	30	III	A. H.	10	
A. O.	13	III			
J. R.	24	II			
J. S.	36				
E. S.	36				
Average 33.9 months			Average 13.7 months		

It may be seen then that most of the Grade I lesions are located in the major bronchi and that most of the less differentiated lesions are located in the smaller bronchi and periphery of the lung. There thus may be two explanations for the fact that Grade III tumors are more rapidly fatal: (1) the rate of growth as measured by cellular dif-

ferentiation, a method which we have shown is open to criticism, and (2) the position of the tumor in the lung. We shall consider the latter in more detail.

Earlier in this paper we gave experimental evidence to show that particulate matter was spread to the regional lymph nodes much more rapidly from the periphery of the lung than from the wall of a major bronchus. From observations at autopsy we were also impressed by the fact that in most of the patients whom we had seen whose first symptoms were from metastatic lesions rather than from the lung, the primary lesion was in the periphery of the lung and often very small.

TABLE V

A COMPARISON OF THE GRADE OF TUMOR WITH THE SITE OF ORIGIN

MAJOR BRONCHUS		MINOR BRONCHUS	
GRADE OF TUMOR	NUMBER OF CASES	GRADE OF TUMOR	NUMBER OF CASES
I	12	I	3
II	9	II	5
III	4	III	7

TABLE VI

NUMBER AND PERCENTAGE OF CASES FOUND IN EACH GRADE

GRADE I		GRADE II		GRADE III	
NUMBER OF CASES	PERCENTAGE OF TOTAL CASES	NUMBER OF CASES	PERCENTAGE OF TOTAL CASES	NUMBER OF CASES	PERCENTAGE OF TOTAL CASES
16	35.5	16	35.5	13	28.6

With no knowledge of the clinical history of the patients we grouped all the tumors in respect to their position of origin, i.e., major bronchus or periphery of lung. That portion of the major bronchus distal to the first bifurcation we termed the periphery of the lung for classification purposes. The clinical records of these patients were then studied, and the length of life was determined from the onset of the first symptoms referable to the lesion until the time of death. It will be seen from Table I that those patients with tumors primary in the major bronchus lived almost four times as long as the other group. In Table IV it can also be seen that those patients whose tumors were visualized bronchoscopically lived on an average of 33.9 months, while those that could not be visualized lived for an average of only 13.7 months.

The explanation of the above findings is one for conjecture. There are probably several factors at play, i.e., increased motion of the lung with massage and pressure changes, greater vascularity, and blood vessels with extremely thin walls, and perhaps to a certain extent the cartilagenous barrier of the larger bronchi.

These pathologic findings verify those obtained experimentally, and we, therefore, feel that a more accurate idea as to the type of course the disease will follow can be obtained if we know the position of the tumor.

DISCUSSION

From the foregoing it can be seen that we prefer to make no detailed genetic classification of primary cancer of the lung other than that of bronchiogenic carcinoma. We feel that the variables and inaccuracies involved offset the even doubtful clinical value of a genetic classification. The situation of cancer of the lung today is not incomparable to that of osteogenic sarcoma a few years past. Until recently one encountered many confusing terms, such as "chondrosarcoma," "spindle-cell sarcoma," "osteosarcoma," etc., and often one tumor would show several of these types. However, they all had their origin in the primitive osteoblast, and the situation was greatly clarified when the simple inclusive term of "osteogenic" sarcoma came into use. Likewise, primary cancers of the lung may present mucous cells, squamous cells, or ciliated cells, but the origin of such cells is from a common parent cell, namely, that found in the basal layer of the bronchial epithelium. For this reason, therefore, we prefer to consider all primary cancers of the lung as bronchiogenic.

As we have shown, the position of the tumor is of great prognostic value. Because of lack of space detailed protocols of our cases have not been given. However, in this series there were eight patients who entered the hospital with no complaint referable to the lungs. Seven of these had cerebral symptoms and one had difficulty in swallowing. Such a condition in which the first evidence of the disease is from a metastasis is obviously hopeless from the start. As has been stated, six of these patients had a primary lesion in the periphery of the lung. With our present methods such lesions will always offer considerable difficulty of diagnosis in their early stages. This is because they will tend to spread early in their course and because they will give little evidence of their presence until this spread takes place.

The progress of the disease and therefore the prognosis of the disease change as the site of origin approaches the major bronchi. In this latter site one encounters a lesion that produces symptoms much earlier, that tends to spread more slowly and thus offers the greatest hope of surgical relief. It must be remembered that most of the symptoms of bronchiogenic carcinoma before it has metastasized are not the symptoms of carcinoma per se but rather its effects, namely, obstruction and ulceration. Like an ulcer elsewhere in the body one of its first signs is hemorrhage, as is evidenced clinically by bloody sputum. The sequelae from obstruction are atelectasis, bronchiectasis, and abscess formation; and these produce such symptoms as dyspnea, pain, cough, and purulent sputum. Generally the larger the bronchus involved the more extensive will be the results of the obstruction and the more pronounced the symptomatology.

Slightly more than one-half of our patients were in this latter class. We cannot but be impressed by the fact that an earlier diagnosis is possible in this group of lesions with the present methods in use. Perhaps one of the commonest errors committed in such cases is that of forgetfulness. It is most important that the frequency of the disease and its manifestations be constantly borne in mind and primary cancer of the bronchus ruled out. The tendency to consider the symptoms as due to tuberculosis or idiopathic bronchiectasis with no thought of carcinoma is at the present time unfortunately widespread.

It is not our intention to discuss treatment of this lesion to any great extent. This has been done elsewhere by others.[6-10] Suffice it to say that the most optimistic results obtained so far have been by surgical removal. Most of the operations have been lobectomies; although total pneumectomy has likewise been successfully performed. The type of operation will of necessity be determined by the requirements of the particular case. In the past the dissection of the regional lymph nodes has been referred to only vaguely. We should like to stress the desirability of the removal of the proper glands as has been discussed in the early part of this paper.

The use of radiation in the form of either local application of radon seeds or as x-ray therapy has been unsatisfactory. Either one or both were used in 18 of our cases. With the exception of sporadic cases of temporary palliation the results have not been encouraging. However, it is only fair to say that all the cases were inoperable and many of them far advanced. It is an interesting fact that several of the patients so treated had tumors that belonged to the so-called Grade III, being composed almost entirely of round cells. This type of tumor gave no more evidence of radiosensitivity than did those composed of more mature cells that were likewise treated. When one realizes the relative radioresistance[11] of the normal bronchial cell, this is not remarkable.

CONCLUSIONS

1. Most, if not all, primary carcinomas of the lung are bronchiogenic. At the present time a more detailed genetic classification is not justified.

2. They tend to extend by the blood stream or by very definite lymphatic pathways.

3. The course of the disease as well as its symptomatology depends to a large extent on the portion of the bronchial tree in which the tumor arises.

4. Tumors of the major bronchi give symptoms earlier, extend more slowly, and are more amenable to surgical treatment.

5. Tumors of the minor bronchi and the lung periphery cause fewer early symptoms and are more rapidly fatal.

6. Histologic grading according to cellular differentiation, while it may offer some information, is subject to various interpretations and inaccuracies and must be used with great care.

Evidence is offered in support of the above statements.

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A TOPOGRAPHIC CLASSIFICATION OF PRIMARY CANCER OF THE LUNG. ITS APPLICATION TO THE OPERATIVE INDICATION AND TREATMENT*

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VARIOUS classifications of primary cancer of the lung have been made by pathologists on the basis of the characteristics of the abnormal cells and the histogenesis of the growth. Our study of more than 250 cases of carcinoma of the lung seen at the Mount Sinai Hospital in the past ten years has led us to conclude that such considerations are as yet of no clinical usefulness. On the other hand, the gross examination of one hundred autopsied cases has indicated leads which we believe to be of clinical value so far as the possibilities of favorable operative treatment are concerned. At the present time the chief interest in carcinoma of the lung centers on the question of surgical removal. We have therefore concentrated our attention on a study of the gross topography and distribution of bronchopulmonary cancer. The selection of the few operative cases to be related is chiefly based on the application of that study to our clinical material. The results suggest, we believe, that an analysis of cancer of the lung along the lines to be indicated should also prove useful to others in whose hands rests the decision as to operability or nonoperability.

There are two points to which we wish to call attention before proceeding with our text. The first is that the great majority of the published cases of operative removal of cancer of the lung are incompletely described. Satisfactory progress in the problem of proper selection of cases for operation will only be possible when the reports of operated cases contain details as to history, roentgenographic features, bronchoscopic examination, regional lymph node involvement, the dissection and microscopic examination of the specimen. The second is that the literature contains descriptions of some operative cases purported but not adequately proved to be cancer of the bronchus. These reports are chiefly concerned with bronchoscopic excision. It is our impression that not a few of the cases to which we refer are instances of nonmalignant tumors (adenomas) of the bronchus. Wessler and one of us (C. R.) called attention to the existence and significance of adenoma of the bronchus two years ago and reported 12 cases.[1] The microscopic features

*From the Laboratories and from the Surgical Service of Dr. Harold Neuhof, Mount Sinai Hospital.

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TABLE I

SITE	INCIDENCE IN 100 AUTOPSIES	REGIONAL LYMPH NODE INVOLVEMENT	ROENTGENOGRAPHIC FEATURES	BRONCHOSCOPY	CHARACTERISTIC SYMPTOMS
Cancer of the Lung—Circumscribed Type					
1. Parenchymal	9%	Late and limited	Sharply demarcated round shadow, occasionally with fluid level.	Negative for biopsy. Compression of bronchus?	None. Found accidentally or because of late symptoms from local increase in size.
Lobar	3%	Late and limited	Lobar shadow, with or without fluid level.	Negative for biopsy. Compression of bronchus?	None or as above.
2. Peripheral (Branch bronchus localized)	12%	Late and limited	Well-demarcated shadow at surface of lung widening to chest wall, occasionally with fluid level.	Usually negative	Chest pain, local or referred.
Cancer of the Lung—Noncircumscribed Type					
1. Main bronchus Nonstenosing (ulcerating, nonulcerating)	63%	Early	Negative, or root infiltration, or metastatic lesions. (Pleural effusion)	Positive	Cough, hemoptysis, and (or) symptoms of metastases.
Stenosing		Early	Atelectasis, root infiltration, infection of lung or pleura. (Pleural effusion)	Positive	Cough, hemoptysis (?), symptoms of infection, atelectasis, metastases.
2. Branch bronchus	13%	Early	Negative, or metastases, or picture of "unresolved pneumonia." (Pleural effusion)	Usually positive	Symptoms of metastases.

were described as sometimes simulating closely those of carcinoma. It was shown that there was usually a characteristic history and bronchoscopic appearance. The not uncommon incidence of these benign tumors is proved by the fact that 10 additional cases have been encountered at Mount Sinai Hospital since the paper was published. It is of course important to differentiate them from carcinoma of the bronchus in future reports.

In the topographic classification to be presented a sharp separation will be made between localized and nonlocalized types of lesions. This is warranted in the great majority of the cases in the material we have studied. It does not hold true for every case. There are a few instances in which we have been in doubt as to correct classification. Borderline cases are so exceptional, however, that they are only referred to in passing. By and large there is a definite cleavage between the various types to be described.

Some of the descriptive terms which are in use at the present time refer to the origin or assumed origin of the growth, others, to the character of the neoplasm. Those we shall employ are based upon the site and the gross pathologic appearance of the primary tumor. No reference will be made to microscopic characteristics, and there are no implications concerning the much debated alveolar or bronchial source of some neoplasms. By a circumscribed tumor is meant one which has that appearance on gross examination. This term is employed in contrast to a noncircumscribed (or infiltrating) cancer. A main bronchus cancer is one which is situated in and involves the wall of a main bronchus. A branch bronchus cancer grows from one of the divisions of a stem bronchus. By a parenchymal cancer is meant a growth which is situated in the substance of the lung and is not visibly derived from a main bronchus or a macroscopic branch bronchus. A peripheral cancer is situated out near the surface of the lung.

The morphologic study of 100 autopsied cases leads us, like others, to separate them into two great groups, which we term the circumscribed and noncircumscribed forms. Although all are cases of cancer, there is a great contrast in the gross appearance. Whereas the circumscribed form has much of the delimited appearance of a nonmalignant neoplasm, the noncircumscribed variety has the characteristics of the usual invasive form of cancer. The circumscribed type was found in one-quarter and the noncircumscribed type in three-quarters of our cases.

CIRCUMSCRIBED FORMS

1. *Parenchymal cancer* of the lung comprises about half of all the cases of the circumscribed variety. As already stated, the term refers to the situation and not to the source of the growth. The parenchymal tumors are spherical, well-demarcated growths in the substance of the lung, unrelated to macroscopic bronchi. They are so clearly delimited

that tangential sections taken a few millimeters from the neoplasm usually show no infiltration by tumor, even when examined microscopically. The neoplasm appears to grow mainly by expansion rather than by invasion. Rudimentary capsule formation is often to be seen about the growth. This capsule is infiltrated by the proliferating cancer cells. The tumor is usually not large and the lymphatic channels appear to be free from cancer cells. Even at autopsy the regional lymph nodes may be uninvolved microscopically. When lymph node metastases exist, they are limited and are apparently due to the sporadic entrance of neoplastic cells into lymph vessels rather than to constant permeation of these channels. Patients suffering from parenchymal tumors die of distant blood-borne metastases and not of the pulmonary neoplasm. The characteristics which have been described obviously class parenchymal tumors as a most favorable variety for surgical removal.

In a small percentage of the cases of parenchymal cancer the growth assumes large proportions and, at postmortem examination, occupies all or almost all of the lobe of the lung. We have termed this variety the lobar type. The occurrence of such large growths with little or no involvement of the lymph nodes in all the cases which have come under our observation indicates that in these cases also there is very little tendency for the neoplasm to spread along lymphatic channels. Autopsy examination leads to the impression that these growths, too, can be placed in the class in which radical extirpation may be feasible.

2. *Peripheral Cancer.* (*Branch bronchus localized type.*) The remaining half of the circumscribed cases of cancer of the lung belongs in this group. The tumors originate from branch bronchi of medium to small size, and the direction of their growth is outward. They are of a more infiltrative nature but are unique because the infiltration progresses peripherally. They form a dense mass of neoplastic tissue which is sharply circumscribed on its central aspect but which invades the lung peripherally to the pleura. In many cases the invasion extends through the pleura to involve the chest wall or diaphragm and may partially destroy overlying ribs. In spite of the peripherally diffuse or invasive characteristic the central limits of the growth remain sharply circumscribed so that sections taken just mesial to the neoplasm are usually free of carcinomatous invasion. Another feature of branch bronchus peripheral carcinoma is the slight or only moderate and late invasion of regional lymph nodes. In a number of the autopsied cases no lymphatic metastases could be demonstrated. This group, too, falls into the class in which operative treatment has favorable possibilities.

NONCIRCUMSCRIBED FORMS

Main bronchus and *branch bronchus* tumors account for all the carcinomas of the lung of the noncircumscribed or infiltrating type, and comprise three-quarters of the total number of cases. All the neoplasms

arising from main bronchi or from main bronchi to lobes fall into this group. Included as well are about half the neoplasms arising from branch bronchi. Characteristic invasive features were found in almost all the cases at autopsy. The regional lymph node involvement was usually massive. The lesion in the main bronchus cancers was ulcerating in some instances, flat and submucosal in others. The well-known characteristics of the stenosing variety of main bronchus tumors require no repetition. In contrast to the branch bronchus localized type which is only peripherally invasive, the noncircumscribed form of branch bronchus cancer presents widespread central invasion. As compared with the localized forms which have been described, these bronchus cancers as a whole show the striking contrast not only of spread but also of extensive and (presumably) early regional lymph node involvement. It is a permeating form of cancer as compared with what might be termed the accident of spread of the localized type. An analysis of the autopsied cases indicates that the lesion was in a sufficiently limited form, possibly amenable to surgical eradication, in only a few instances. The same statement holds true for the many clinical cases which have come under our observation. The literature proves that there are exceptions. From our material we can only conclude that the great majority of patients with main bronchus cancers are not operable by the time they become sufficiently ill to enter the hospital or clinic.

Some additional data can be added as the result of the combined clinical and postmortem studies of our material. They may be summarized as follows:

1. Except in rare instances the parenchymal type of neoplasm grows concentrically and by expansion and does not change into an infiltrating or noncircumscribed type.

2. In only two of the localized neoplasms in our series were there lymph node metastases demonstrable clinically or radiologically.

3. In the noncircumscribed type of neoplasm there are clinical and (or) radiographic evidences of involvement of the mediastinal or cervical lymph nodes in a large proportion of the cases by the time patients come under hospital observation.

4. In the instances of the noncircumscribed type in which there was no clinical or roentgenologic evidence of lymph node involvement during life, widespread metastases were found at necropsy.

5. In cases of bronchus cancer which presented a negative roentgenogram shortly before death the regional lymph nodes were found extensively involved at necropsy.

A consideration of the foregoing leads to an alternative topographic classification which may perhaps be termed a surgical one. In such a classification, designed for operative purposes, cancers of the lung would be grouped into two classes: (1) tumors of the lung root zone and

(2) tumors of the parenchymal zone. In the first group would be placed the large bronchus neoplasms. These would generally fall into the inoperable class. In the tumors of the parenchymal zone would be placed, first, the compact tumors occupying more or less of the lobe; second, the peripheral tumors which are essentially peripherally invasive. These two groups would fall in the more favorable operative class. There would remain a small group of secondary and tertiary bronchus tumors which occupy the parenchymal zone, but are centrally invasive and therefore are in the same class as the tumors of the lung root zone.

The symptoms, roentgenologic and bronchoscopic features of lung tumors will now be linked up with the various topographic forms. To enter into details would take us too far afield. We shall limit ourselves to distinctive characteristics in order to show that the varieties which have been described can and should be recognized as such clinically.

SYMPTOMS

Cough and hemoptysis result from the ulceration of tumors of the larger bronchi or from infection of the lung beyond an obstructing tumor to one of these bronchi. In the absence of these or other local complicating factors evidence of the presence of the neoplasm is dependent upon the altered general condition, clubbing of the fingers, and the symptoms of metastases. Cough is a symptom which depends largely upon the involvement of the larger bronchi; and although it is absent in the main bronchus tumors which are nonulcerating and nonstenosing, it constitutes one of the earliest symptoms in this group of pulmonary new-growths. On the other hand, in the case of the peripheral or parenchymal tumors, cough either is entirely absent or occurs as a late symptom from pressure on the main bronchi. Extensive invasion of the mediastinum may be the first evidence and the first source of the symptoms of a noncircumscribed cancer of the smaller bronchi. Similarly, carcinomatous lymphangitis of the pleura with a bloody pleural effusion results from peripheral permeation and may thereby be the source of the first symptoms of a noncircumscribed cancer of smaller or larger bronchi.

The most common signal symptom of the circumscribed tumors of the smaller bronchi (peripheral carcinoma) is pain. It is due to the peripheral spread of the neoplasm and its gradual extension to the pleura and to extrapleural structures. The pain is localized at first but at a later stage may be referred to various nerve pathways. As the growth progresses it often involves the overlying rib. Local tenderness may be found as well as hyperalgesia along the course of the corresponding intercostal nerve.

The parenchymal neoplasms usually cause no local symptoms and, because they are situated beneath the surface of the lung, rarely induce abnormal physical signs. Only when they attain considerable size do they cause cough from pressure on the bronchi or give rise to pain from involvement of the pleura. The symptoms are only a general feeling of ill health and loss of weight, or the first signs may be referable to a distant, blood-borne metastasis. Clubbing of the fingers which usually occurs early in this, as well as in the other types of neoplasms, may be the only lead to the diagnosis.

Fig. 1.—Parenchymal type. Case 5. Sharply circumscribed neoplasm in upper part of left lower lobe. The shadow at the left hilum represents the pulmonary artery. Lymph nodes uninvolved.

RADIOGRAPHIC FEATURES

The roentgen examination of the chest furnishes the most reliable method for the diagnosis of the localized types of neoplasms. The parenchymal neoplasms are sharply demarcated, round shadows which may be situated anywhere within the pulmonary fields. Occasionally they present a fluid level which may simulate the shadow of a lung abscess. The differentiation may be most difficult from the roentgen examination alone, but the absence of foul sputum as well as the bronchoscopic and the bronchographic characteristics of lung abscess should indicate the true nature of the lesion. In the case of the large parenchymal neo-

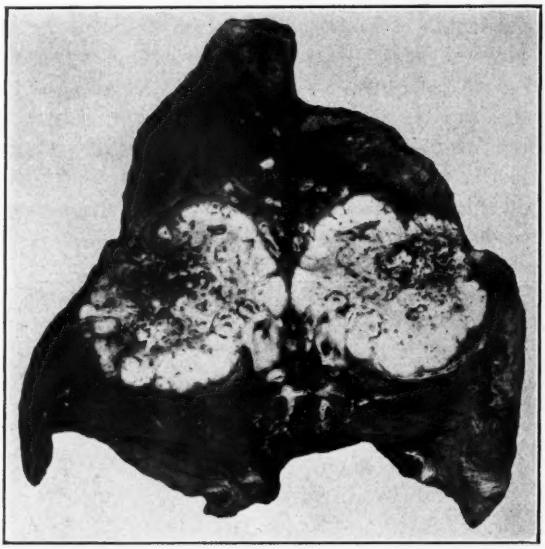

Fig. 2.—Parenchymal type. Case 5. Lobectomy specimen showing sharply circumscribed neoplasm of left lower lobe. The large bronchus is compressed but not infiltrated by the neoplasm.

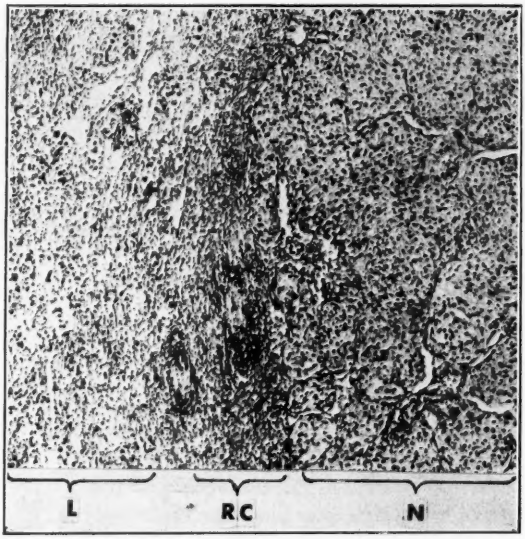

Fig. 3.—Low power photomicrograph of border of parenchymal neoplasm. Case 5. The rudimentary capsule is composed of anthracotic connective tissue and compressed lung. There is no evidence of capsular infiltration in this section. *N*, neoplasm; *RC*, rudimentary capsule; *L*, adjacent lung.

plasms which occupy an entire lobe, the picture may be confused with that of an ordinary consolidation. The convex border of the shadow of a lobar neoplasm, however, serves to differentiate it from a pneumonic consolidation.

The circumscribed tumors of the branch bronchi (peripheral tumors) cast well-demarcated shadows extending to the surface of the lung, widening as they reach the chest wall. Careful inspection may disclose more or less complete destruction of a rib. These neoplasms break down and discharge their contents into the bronchi more frequently than do

Fig. 4.—Parenchymal (lobar) type. Autopsy specimen of right lung. The entire upper lobe is replaced by a sharply circumscribed lobar carcinoma. Note absence of lymph node involvement.

the parenchymal growths and then simulate the radiographic appearance of a lung abscess.

The roentgen picture of the main bronchus tumors is dependent upon the presence or absence of bronchostenosis. The typical evidence of atelectasis in bronchostenosing tumors requires no comment. When infection supervenes, the appearance is that of a pulmonary or pleural suppuration. If the neoplasm is not bronchostenosing, its manner of infiltration of the lung may be observed from the roentgen film. There are infiltrating shadows most dense at the root of the lung and extend-

ing in fine streaks and nodules toward the periphery. Usually the shadows of enlarged mediastinal lymph nodes are visible. Occasionally the lesion at the root may be obscured by the heart, pulmonary vessels, and mediastinal structures so that the film is entirely negative.

The noncircumscribed neoplasms of the smaller bronchi usually present the appearance seen in unresolved pneumonia (at relatively early stages of growth). Later, a lymphangitic carcinosis of both lungs often supervenes. The film then shows the lungs to be occupied by fine streaks

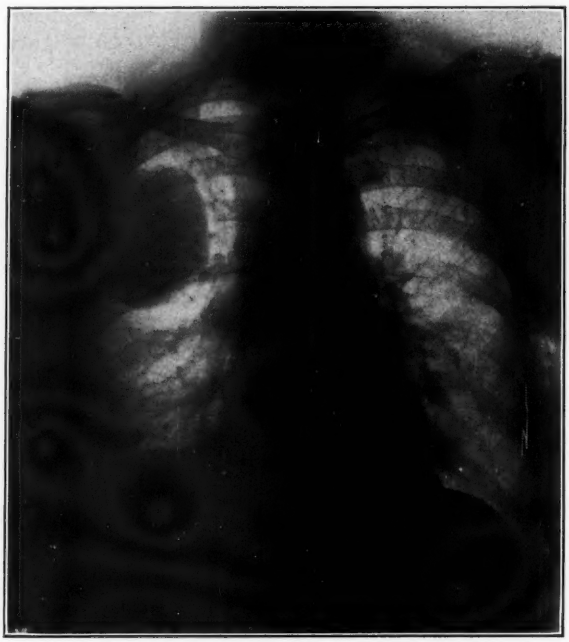

Fig. 5.—Branch bronchus localized (peripheral) type. Case 4. Showing sharp demarcation on central aspect of the growth and absence of lymph node involvement.

and nodules, and the primary growth may not be recognizable. A carcinomatous involvement of the pleura with pleural effusion may occur early in the disease.

BRONCHOSCOPIC FEATURES

Tumors of the main bronchi are always visible and present themselves either as fungating excrescences, flat nodules, or as a diffuse thickening of the walls of the bronchi. It is important to note that the absence of an ulcerating or bronchostenosing lesion does not exclude the existence of a main bronchus cancer. Many of our cases have been diagnosed correctly only on the basis of adequate specimens removed from suspicious and not characteristic lesions. Bronchoscopic biopsy may

have to be repeated before a positive microscopic diagnosis can be made. The noncircumscribed type of branch bronchus carcinoma usually begins in a branch too small for entry of a bronchoscope. By the time bronchoscopy is performed, however, the growth has usually extended centrally to a spur. A positive diagnosis from a specimen removed at a bifurcation can therefore usually be made.

Although it is conceivable that a localized branch bronchus neoplasm (peripheral tumor) may be visible through the bronchoscope, the great majority of those which have come under our observation have been

Fig. 6.—Branch bronchus localized (peripheral) type. Case 4. Lobectomy specimen showing neoplasm circumscribed on its central aspect but infiltrating the ribs (*R*) peripherally.

situated too far down the bronchial tree to be seen. It is evident that the parenchymal type which has no grossly visible connection with the bronchial tree even at necropsy, cannot be seen directly. The presence of either of these circumscribed forms can sometimes be inferred because of the distortion of the bronchial tree by external pressure.

The value of bronchoscopy in determining the situation and the type of neoplasm is obvious. Disregarding the unusual instance of a visible localized branch bronchus tumor or the equally rare incidence of an

invisible branch bronchus noncircumscribed cancer, visualization of the neoplasm through the bronchoscope is usually indicative of a noncircumscribed, infiltrating growth and nonvisualization is indicative of a circumscribed neoplasm. The extraordinary precise information derived from well-conducted bronchoscopic studies in carcinoma of the lung is to be noted in an analysis of the material of Mount Sinai Hospital made by Doctors Kramer and Som, to be published shortly. Of bronchoscopic examinations in a hundred patients who subsequently came to autopsy, there were positive findings and positive biopsy in 72 cases. All proved to be noncircumscribed cancers of the bronchi. Of the 28 remaining

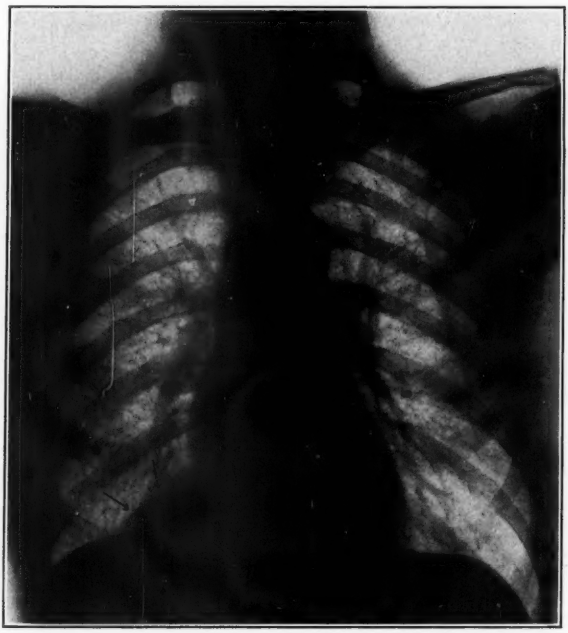

Fig. 7.—Branch bronchus localized (peripheral) type. Case 3. The neoplasm is situated behind the dome of the diaphragm. Its upper border is seen in the right cardiophrenic angle. No evidence of lymph node involvement.

cases, the autopsies revealed that 20 were parenchymal tumors, 6 were small branch localized (peripheral) tumors, and two were noncircumscribed cancers in which occluding cancerous lymph nodes blocked entry of the bronchoscope.

INDICATIONS FOR OPERATION BASED ON THE TOPOGRAPHIC CLASSIFICATION

Any delay in proceeding with operation in the favorable types of cancer of the lung is inexcusable in view of the ever present likelihood of the accident of blood stream metastasis. The lymphatic extension

which occurs in the less favorable types is probably a more or less constant phenomenon, and the same imperative argument for prompt action cannot perhaps be advanced for this class of cases. In any event the necessary studies to determine whether the pulmonary lesion is a primary one require little time, and there is surely no justification for prolonged attempts with radiotherapy. Operation for the localized forms of neoplasm can be withstood by most patients, even those of advanced age. The more formidable operative procedures which are required for the noncircumscribed forms can be applied only to individuals in fair or in good condition. From the analysis of our material we are led

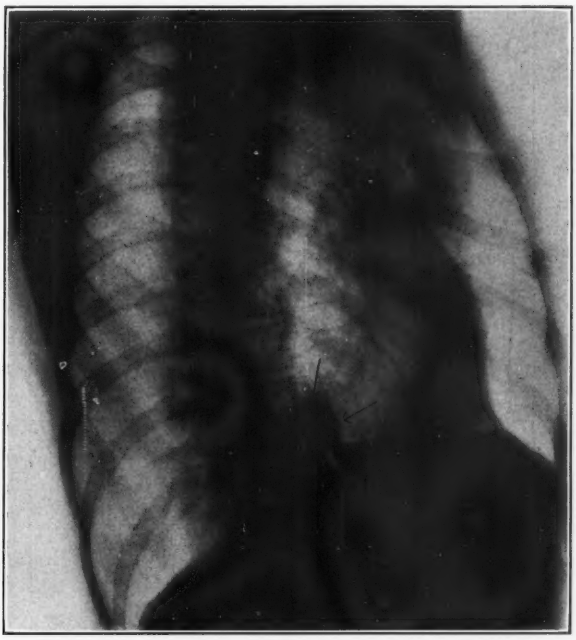

Fig. 8.—Oblique view of same case. Showing circumscribed neoplasm adherent to the posterior portion of the right leaf of the diaphragm. The posterior mediastinum is clear.

to urge, for the time being at any rate, that more attention should be devoted to the localized forms of pulmonary cancer even though they comprise only a quarter of all cases. The only contraindication to operation in this group is the presence of metastases or the obvious inability of the patient to withstand the operation. Total lobectomy is not essential for a branch bronchus localized type; a partial pneumonectomy may suffice for a parenchymal cancer. It may be argued that the circumscribed forms of pulmonary cancer are not likely to be recognized at an early date because of the silent course they often pursue. Late-

ness of time should not be confused with lateness so far as operability is concerned. On the whole, the noncircumscribed main bronchus tumors induce symptoms early in the disease from the standpoint of time, yet many are inoperable, in our experience, soon after the onset of the initial symptoms. In other words, they are already late from the viewpoint of the extension of the growth. We do not wish to be understood as decrying efforts at earlier recognition of either of the forms of pulmonary cancer. On the contrary, more prompt bronchoscopic ex-

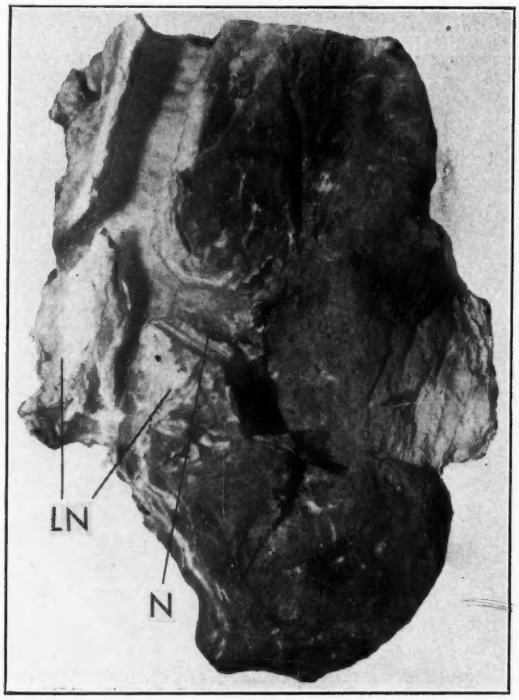

Fig. 9.—Main bronchus type. Autopsy specimen right lung; trachea and bronchi opened posteriorly showing ulcerating neoplasm (*N*) of right upper lobe bronchus. Note involvement of paratracheal interbroncheal and tracheobronchial lymph nodes by carcinoma (*LN*); negative roentgenogram.

amination of patients suffering from cough of undetermined origin will doubtless disclose neoplasms of the larger bronchi at an earlier stage than they are found at the present time. Similarly, the earlier use of fluoroscopy and radiography in patients with obscure chest symptoms, particularly in those with clubbed fingers, will reveal localized tumors before they have attained great size. At the present time, however, the stand we have taken, based on a study of more than 250 cases, appears warranted.

OPERATIVE TREATMENT BASED ON THE TOPOGRAPHIC CLASSIFICATION

Five operative cases with which we wish to illustrate our text have been reported elsewhere.[2] They are presented here briefly because of morphologic features and not for technical consideration. The first is a main bronchus cancer. With a month's history of fever, cough, and blood-streaked sputum the patient entered the hospital. After several weeks' observation a bronchoscopy was performed, and a cancer of the lower lobe bronchus, an inch below the orifice of the upper lobe bronchus, was noted. At operation a high lobectomy was carried out for the large bronchostenosing tumor. There were apparently no involved hilar

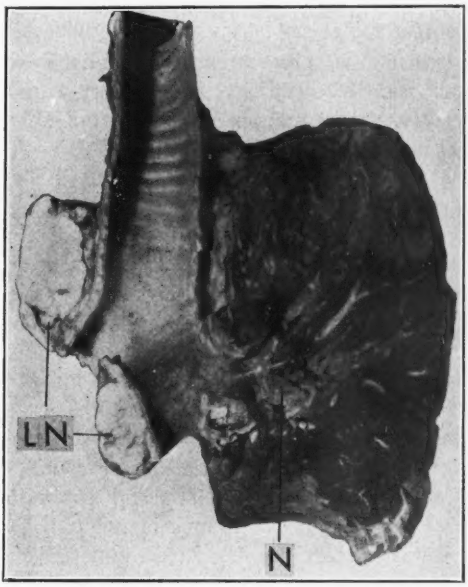

Fig. 10.—Branch bronchus infiltrating type. Autopsy specimen upper lobe of right lung; trachea and bronchi opened posteriorly showing irregular neoplasm (*N*) in axillary branch of right upper lobe bronchus. Note involvement of interbronchial and paratracheal lymph nodes (*LN*) and submucous infiltration of main bronchus by the carcinoma. Neither the primary neoplasm, nor the involved lymph nodes could be visualized on the roentgenograms.

lymph nodes, but a metastatic node was found on the descending aorta after the tumor was removed. The course was satisfactory for a few months. Five months after operation the patient returned to the hospital with evidences of spinal metastases. He died with the picture of widespread regional and distant metastases, which was confirmed by autopsy.

The second case was a localized tumor of the right lower lobe which was accidentally noted three years before in a roentgenogram of the chest taken because of symptoms referable to gallbladder disease. Only

a year later did cough and asthenia appear. The subsequent course was characterized by fever and pain in the right upper abdomen. Roentgenograms were made at frequent intervals and demonstrated the progressive expansion of the circular shadow in the right lower lobe. Backache first began shortly before hospital admission, but operation was proceeded with, three years after the neoplasm had been discovered, because there were no objective evidences of a spinal metastasis. At operation the bilocular cancer in the substance of the lower lobe extended peripherally to invade the diaphragm. It was excised together with the involved portion of the diaphragm. There was no demonstrable regional lymph node involvement. Objective evidences of a spinal metastasis were noted several weeks after operation, and the patient died with the picture of a spinal metastasis about six months later.

The third case came under observation with localized pain in the right lower chest of six months' duration. Some asthenia and dyspnea appeared more recently. There was considerable loss of weight. Clubbing of the fingers was noted a month after the onset of pain. The roentgenogram revealed a well-demarcated peripheral shadow abutting on the diaphragm posteriorly. Bronchoscopy was negative. At operation a cancer which broadly invaded the chest wall and diaphragm was released by the sacrifice of several ribs and a portion of the diaphragm. Its origin from the lung was so superficial that a partial pneumonectomy appeared sufficient. There was no demonstrable regional lymph node involvement. The patient did well for nine months. At the end of that time the objective evidences of a cerebral metastasis appeared. The cerebral lesion was the cause of death. At the postmortem examination there was no local recurrence and no involved regional lymph nodes. The only cancerous deposits which were found in a complete autopsy were a solitary cerebral metastasis and a minute adrenal one.

The fourth case was also one of branch bronchus peripheral cancer. The lesion, which was of large size, was in the upper lobe and the roentgenogram was characteristic. The symptoms, of ten months' duration, were not distinctive of this type of neoplasm. They were a combination of pain, cough, dyspnea, and severe precordial pain. At operation the widespread invasion of the posterior chest wall required sacrifice of portions of the upper five ribs. The hilum was free from involvement. A lobectomy was performed. Death occurred suddenly on the third day. At the postmortem examination an entirely unsuspected and severe adhesive pericarditis was found, as well as a perihepatitis. There was no regional lymph node and no distant metastases.

The fifth case was a parenchymal cancer of the left lower lobe with symptoms of six months' duration. The symptoms suggested recurring episodes of pneumonitis. Toward the end of the six months' period, pain in the left chest and asthenia appeared. The roentgenogram revealed a characteristic circular shadow, and the bronchoscopy was nega-

tive except for the evidence of extrabronchial pressure. At operation the spherical tumor at first appeared to involve the hilum but was found only to have grown up to surround it. There was no regional lymph node involvement. A lobectomy was performed. The course has been satisfactory for more than a year since operation. When seen recently the patient presented symptoms suggestive of a cerebral metastasis. There was no clinical or roentgenologic evidence of a local recurrence.

An extended comment on these five cases is unnecessary. They illustrate the points which were made in the topographic classification. In particular, they demonstrate that a main bronchus tumor of relatively limited proportions was characterized by widespread central invasion. On the other hand, larger parenchymal tumors presented no evidence of lymphatic extension, and peripheral tumors which widely invaded the parietes were also entirely free from lymph node involvement.

SUMMARY

The present-day interest in cancer of the lung centers on the question of operative removal.

A study was made of 250 cases of primary cancer of the lung, in which 100 autopsies were done, with the object of classification for clinical purposes.

Only the gross topographic features of cancer of the lung proved to be of aid in classification as to probable operability or probable nonoperability.

Two main groups, termed the circumscribed and the noncircumscribed types, are identified and described.

The circumscribed type comprises a fourth of the cases. Cancers of the circumscribed type occupy the parenchymal and peripheral zones and are termed parenchymal and peripheral tumors. Regional lymph node involvement occurs late and is limited. The peripheral tumors grow from branch bronchi and may therefore be termed branch bronchus circumscribed tumors.

The noncircumscribed type, to which three-fourths of pulmonary cancers belong, comprises tumors growing from main and from branch bronchi. These neoplasms are termed main bronchus and branch bronchus tumors. They present the usual invasive characteristics of cancer in the great majority of cases.

Clinical, radiographic and bronchoscopic features are described. They serve to differentiate the circumscribed from the noncircumscribed types. The diagnosis as to type can be accurately made on the basis of these features.

Peripheral (branch bronchus localized type) and parenchymal tumors tend to fall into the class of operability. On the other hand, the great majority of main bronchus and branch bronchus tumors (with the

exception of the peripheral type) do not fall into the operable class, in the sense of surgical eradication, at the time at which patients suffering from these lesions ordinarily come under observation.

The indications for operation, based on the topographic classification, are outlined. Five operative cases are described as illustrations of the selection of cases for operative treatment on the basis of topographic features.

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BRONCHIAL CARCINOMA

Bronchoscopic Biopsy in a Series of 32 Cases*†

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THIS presentation is based on a review of cases seen at the Temple University Hospital during the past four and one-half years. In that time we have seen thirty-two cases of bronchopulmonary cancer in which bronchoscopic biopsy was confirmative. In all of these cases but three the endobronchial lesion was thought to be primary. It may be of interest, in connection with the apparently increased incidence of bronchial carcinoma, to note that there were four cases in 1930, five cases in 1931, eight cases in 1932, and ten cases in 1933.

Bronchoscopy now occupies a secure place in thoracic surgery; it has come to be accepted as an important diagnostic and therapeutic procedure.[8] The cardinal indication for diagnostic bronchoscopy is clinical or roentgenologic evidence of bronchial obstruction (a wheeze, or an area of obstructive atelectasis or obstructive emphysema), and in no connection is it more valuable than in the early diagnosis of bronchial carcinoma. Almost twenty years ago, Chevalier Jackson removed bronchoscopically a tumor diagnosed an "endothelioma" by the pathologist. In the report of this case[9] and subsequent papers[10, 11, 12, 13] and textbooks[14, 15] he has emphasized the diagnostic possibilities of the bronchoscope as an aid to the thoracic surgeon in the early and accurate diagnosis of endobronchial neoplasms.

It is very gratifying to those of us interested especially in bronchoscopy to note that in Graham's recent case of successful pneumonectomy,[7] bronchoscopic biopsy had been done by Arbuckle; and that likewise, in Churchill's case of lobectomy[4] in which both the right lower and the middle lobes were removed, bronchoscopic biopsy had been done by Rice.[22] Archibald, in discussing Churchill's paper, expressed the hope that more and more cases of bronchial carcinoma would be diagnosed early, "because such growths soon give rise to the symptom of unproductive cough, which leads necessarily nowadays to bronchoscopy and so to diagnosis."[4] In addition to affording means of diagnosis, with or

*From the Bronchoscopic Clinic and the Laboratories of the Temple University Hospital, Philadelphia.

†Read at the Seventeenth Annual Meeting of the American Association for Thoracic Surgery, Boston, May 31, 1934.

‡Since reading this paper, I requested Dr. Frank W. Konzelmann, pathologist to the Temple University Hospital, who had examined all the sections, to write a discussion of the pathology, grading, and classification of these tumors. His discussion is incorporated in this joint article, with the permission of the Editor. (C.L.J.)

without biopsy, bronchoscopy will give the surgeon "definite evidence regarding the level at which the lobe or lobes must be amputated to reach the upper limits of the tumor" (Churchill). Carlson and Ballon[1] regard bronchoscopy and bronchoscopic biopsy as of the greatest value, not only in early diagnosis, but also in the decision as to operability and type of operation.

The internists as well as the surgeons have come to recognize the value of bronchoscopy in the diagnosis of bronchopulmonary neoplasms. Miller[17] stated, in 1930, that on his service at the Bellevue Hospital, bronchoscopy was never omitted in the study of chest cases with negative sputum, especially if the patient was over forty years of age. A series of thirty-two proved cases is reported by Miller, of which fifteen had positive bronchoscopic biopsies. At the Mayo Clinic, according to Vinson,[24] bronchoscopy has become "almost a routine procedure in the study of patients with cough and expectoration or pulmonary hemorrhage, if the usual methods have failed to reveal the presence of tuberculous disease in the lungs." Fried, in his monograph,[6] speaks highly of bronchoscopic biopsy, and in many of the cases that he reports positive biopsies had confirmed the diagnosis. Kernan[16] has reported an interesting series of cases diagnosed by bronchoscopic biopsy and treated by bronchoscopic diathermy and radon implantation.

European and other foreign literature has contained many references to the value of bronchoscopy in the diagnosis of bronchopulmonary neoplasms. Soulas[23] in Paris, Peroni[21] in Milan, and Von Eicken[25] in Berlin have all reported cases in which bronchoscopic biopsy was done. In England, Negus,[19] Nelson, Tudor Edwards, Ormerod,[20] Thacker-

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PLATE I

BRONCHOSCOPIC VIEWS OF BRONCHIAL CARCINOMA

1. Nodular lesion partially obstructing the right lower lobe bronchus. Note orifice of right upper lobe bronchus at right and that of middle lobe bronchus above. (Case 19.)
2. Tumor mass completely obstructing the left lower lobe bronchus in a woman thirty-four years of age. Note orifice of left upper lobe bronchus in left upper quadrant. (Case 15.)
3. Middle and right lower lobe bronchi partially obstructed by an irregular ulcerative lesion which bled easily on contact with the bronchoscope. (Case 20.)
4. Right lower lobe bronchus narrowed, and obstructed by an irregular mass of grayish yellow tissue projecting from its anterior and median walls. Note spur of middle lobe bronchus anteriorly. (Case 13.)
5. Marked thickening of the carina and bulging of the median wall of the left main bronchus. (Case 17.)
6. Right stem bronchus almost completely filled with an irregular bleeding mass, covered with grayish exudate (secondary "clear cell" carcinoma or "hypernephroma"). (Case 18.)
7. Tumor mass partially obstructing the right lower lobe bronchus and extending up toward the orifice of the middle lobe bronchus. (Case 23.)
8. Large mass of tumor tissue obstructing the left main bronchus and causing atelectasis of the entire left lung. (Case 26.)
9. Lumen of right stem bronchus markedly narrowed by encroachment of its median wall, which prevented full exposure of the orifice of the middle lobe bronchus. The surface of the bulging median wall is somewhat nodular. (Case 10.)
10. Fungation projecting from depths of left upper lobe bronchus. (Case 9.)
11. Orifice of right main bronchus involved in a bleeding ulcerative lesion which apparently originated in the right upper lobe bronchus and has caused almost complete obstruction of it. (Previous diagnosis pulmonary tuberculosis.) (Case 11.)
12. Left bronchus completely obstructed by soft fungations and blood-stained mucopurulent secretions in a young girl (aged twenty years). Left lung was found to be completely atelectatic but chief complaint was "weakness of ankles," due to secondary lesion in thoracic vertebrae. (Case 28.)

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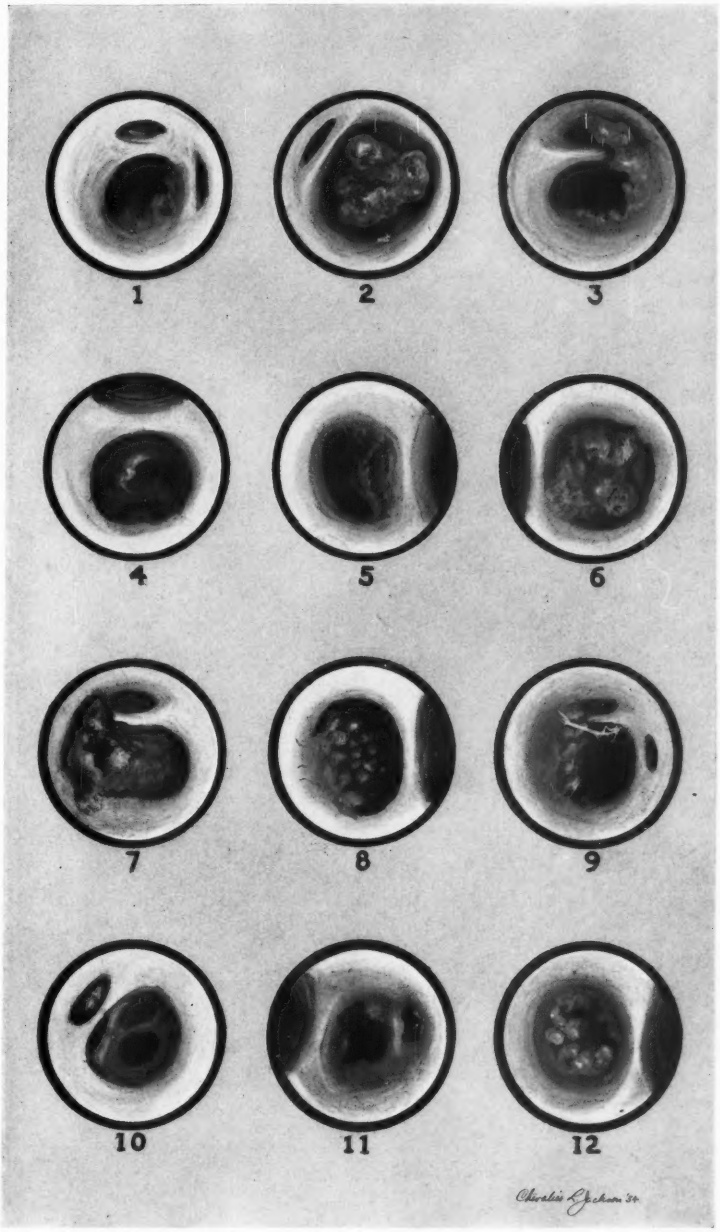


PLATE I

Neville, and others have written favorably of bronchoscopic aid in diagnosis. In Cuba some excellent work has been done by a group of men who have reported an interesting series of cases with well-correlated clinical, roentgenologic, bronchoscopic and anatomicopathologic studies. These workers (Castillo, Basterrechea and Fariñas[2]) call attention to the fact that it is logical to study especially the *bronchi*, by bronchography and bronchoscopy, in the diagnosis of pulmonary carcinoma, since it is the consensus of opinion that from 75 to 90 per cent of the cases are bronchial in origin. Another Cuban writer (Navarrete[18]) likewise stresses the importance of bronchoscopic examination.

TECHNIC OF BIOPSY

After careful roentgenographic localization of the lesion in both planes, the bronchoscope is passed down to the suspected area and the bronchial orifices are inspected. If fungating tissue is found in any of them, removal of an ample amount is easy. For this type of lesion we generally use a light "ball" forceps. If the lesion is rather of the infiltrative type, it may be necessary to use a cutting "tissue forceps." Of course, if there is no definite involvement of the bronchial wall, but only a compression or bulge, biopsy should be postponed. One should exercise great care not to traumatize normal bronchial spurs nor to bite too deeply. It is necessary to inspect the lesion carefully and to make certain to get tissue representative of the tumor itself and not just the peripheral "inflammatory zone." In many of the cases exuberant granulations are produced in the vicinity of the lesion and, of course, tissue removed from these will not show the growth. As was first mentioned by Chevalier Jackson, and recently emphasized by Clerf and Crawford,[3] it is very important that the bronchoscopic picture be carefully studied, and particularly that the presence or absence of distortion, fixity and infiltration of the bronchial wall be noted. This is especially important when the histologic picture is inconclusive, though in such cases additional biopsies will generally give more definite histopathologic information. Care should be exercised, when removing specimens of tissue from the jaws of the specimen forceps, that they are not unduly crushed in gauze; the specimens should be picked up with delicate thumb forceps and placed at once in a small bottle already filled with a solution of formol alcohol.

PATHOLOGY AND CLASSIFICATION

The intent of this presentation does not call for a consideration of the gross morbid anatomy of bronchopulmonary carcinoma other than the changes seen through the bronchoscope. Of late, much interest has been manifested in the histopathology of these morbid growths. Many classifications of them have been suggested, some simple, others elaborate.

One cannot consider the subject without turning to Dr. Ewing's logical grouping, which is as follows:

a. Carcinoma arising in the lining cells of the bronchus.
b. Carcinoma arising in the mucous glands of the bronchus.
c. Carcinoma which arises in the pulmonary alveoli.

Theoretically, a carcinoma could not arise in any other tissue of the lung unless it be ectopic epithelium. Doubt has been expressed by many observers of the existence of an epithelial lining in the pulmonary vesicle. Fried[6] and others would have us believe that after birth the cells lining the alveolus are phagocytic reticuloendothelial cells. We do not subscribe to this hypothesis. We believe rather with W. S. Miller as he writes in *Special Cytology*[5] that the epithelium of the respiratory bronchiole extends through the alveolar ducts to the pulmonary alveolus, where it appears as thin, flattened, nucleated squames, which form a continuous lining. It does not follow that because these cells are flat, they are endowed with the ability to produce keratin or that they are any more likely to give rise to squamous cell carcinomas than those cells found anywhere in the tracheobronchial tree. There is no evidence that these cells are capable of regeneration or of multiplication; but, when they are destroyed, a new lining membrane could be formed from the basal generative cells found in the bronchiole.

Even if these adult differentiated elements lining the alveolus did give rise to a malignant tumor, there is no reason to believe that such a tumor would have any different characteristics from those tumors arising anywhere else in the bronchial tree. The lining cells are embryologically the same and endowed with the same potentialities. The problem is thereby reduced to the supposition that all primary pulmonary carcinomas are bronchogenic.

The remaining two classes mentioned above can be distinguished with difficulty, if at all, so in the interest of prognosis and treatment one seeks variations in gross and microscopic morphology which might with regularity coincide with some constant feature of the disease.

Fried's analysis of the histologic features and embryology is rational. It coincides in part with what we have observed in the study of the 29 primary cases reviewed in this series. He calls attention to the presence of a basal generative cell which normally gives rise to ciliated and goblet cells characteristic of the bronchial mucosa. He calls them, properly, postembryonic undifferentiated cells and reminds us of their close relationship embryologically to the basal or generative cells of the esophagus. In the environment of the bronchus these cells produce columnar epithelium or gland cells; while in the environment of the esophagus, cells which have a common embryologic ancestry give origin to squamous keratin-producing cells. The belief that all tumors arise from these multipotent cells is much more reasonable than supposing

the adult mature columnar cell to lose one highly differentiated function of mucus production or cilia formation and acquire the new and just as complicated function of keratin production. We do not see the wisdom of considering the appearance of squamous cells in an inflammatory process as a precancerous manifestation. It is on the contrary a protective mechanism which is no less likely to become the nidus of a malignant process than squamous epithelium elsewhere. It does not seem that the observations of Wolbach in vitamin deficiency on the general keratinization of cells is any indication that this protoplasia is necessarily a predecessor of malignancy.

All observers agree upon two classes of bronchogenic neoplasms, viz., adenocarcinoma and squamous cell carcinoma. In pure form these do not differ much from the same classes of tumors seen in other parts of the body. In our series, these two groups represented 21 cases or 70 per cent of the total (exclusive of the three metastatic tumors). They were divided into four groups to facilitate an understanding of the cell types, but not with the idea of suggesting a new classification. The grouping is as follows:

Class A. Frank unquestioned adenocarcinoma, 4 cases. (Figs. 2 and 3.)

Class B. Frank unquestioned squamous cell carcinoma, 7 cases. (Figs. 1 and 9.)

Class C. Frank carcinoma, but the type of cell difficult to establish. The cells seem more mature than the so-called undifferentiated type; they are polymorphous, show neither intercellular spines nor keratin and do not form acini. They occur in more or less solid masses with the cell boundaries lying in contact with one another. The cytoplasm is homogeneous, often lightly basophilic. The nuclei are large in proportion to the cytoplasm but vary greatly in size; frequently there is but a densely stained nuclear membrane and a scant scattering of fine, peppery, deeply stained granules or rods of chromatin. The nucleolus is frequently large and reacts variously to the stain. Mitotic figures vary in number but are frequently numerous and distorted. These tumors are probably classed by many pathologists as adenocarcinoma. Eight cases. (Fig. 6.)

Class D. Combined adenocarcinoma and squamous cell carcinoma. In two cases, we saw cuboidal cells forming fairly typical glands in some areas, while in other areas not far distant intercellular spines and keratin-forming cells were discovered. If we accept the hypothesis that all these cells lining the bronchus are the offspring of basal cells, and that under certain circumstances they form either cylindric cells or squamous cells, it is not surprising that under the peculiar circumstances that surround tumor formation some cells will mature as they would normally, and others develop the special function of keratinization. It is most likely that the majority of observers would recognize this class as squamous cell carcinoma. Two cases. (Figs. 4 and 5.)

The remaining 30 per cent consist of anaplastic cells that are called by Clerf and Crawford[3] undifferentiated cells. This group seems to include also the two classes of Fried, which he called medullary carcinoma and basal cell carcinoma. In our own studies, we recognized two classes similar to those of Fried:

Class E. Diffuse infiltration of cells that are small, round or polyhedral and with little cytoplasm. They lie loose, unattached to one another, in a very scant stroma.

The nuclei are round or oval. The nuclear membrane is not so distinct, yet recognizable. The chromatin is more abundant than in the nuclei of Types A, B and C. It is distributed in the form of peppery granules. Nucleoli are small or absent in all but one case. Mitotic figures are seen in moderate numbers. This is the medullary carcinoma of Fried and one that has been frequently erroneously called sarcoma or lymphosarcoma of the lung. There are four cases of this class. (Fig. 7.)

Class F. The cells are similar to the cells of Class E, in that they are round or polyhedral. But the stroma is more abundant and the cells tend to form cords or long tubes or to cling to the walls of poorly formed spaces in the stroma. This is the class that might be mistaken for an alveolar sarcoma. We believe it is the same as Class E, the cells showing a little more differentiation or a little less anaplasia. It corresponds to the basal cell bronchopulmonary carcinoma of Fried.

We are not convinced of the value of subdivision of this group of cases. If future experience will establish the constancy of Fried's observation, that the medullary class metastasize early to the liver and the basal cell class rarely metastasize and may be controlled by x-ray treatment, we shall have a very valuable guide to prognosis and treatment. In this particular group the variation of cell structure is so great in different parts of the tumor that it is not either practical or accurate to look upon subdivisions as any more than an estimation of the degree of anaplasia.

There was little difference, so far as prognosis was concerned, in any of our cases; 18 of the 29 are dead, 3 are living, and 8 could not be traced. The longest duration of life after the appearance of symptoms was eighteen months, while the shortest was three months. The patients still living are the most recent.

We believe that the importance of biopsy is not only to confirm a clinical diagnosis but to establish a diagnosis in cases in which neoplasm has not been suspected. It will not alone decide the course of treatment. It has been our practice to correlate the information obtained by bronchoscopy, roentgenography and microscopic study of biopsy material. The sum of these three indicates the course to be pursued. We understand that a malignant lesion may occasionally be recognized early and be completely removed by the aid of a bronchoscope, and that such tumors may not recur, or if the affected lobe is removed, no further evidence of carcinoma will be found. Certainly no one can doubt the presence of malignancy in the cases reported by Kernan as being free of evidence of recurrence after two and three years. That these patients have been permanently cured is open to question, but the failure of recurrence does not imply an erroneous diagnosis of malignancy. Biopsy can distinguish for us inflammation, benign and malignant growths. Roentgenography and bronchoscopy must guide us in therapeusis.

Complicated classifications, while of statistical value, cloud the issue and certainly up until now have not helped in either prognosis or treat-

ment. In the Chevalier Jackson Clinic, bronchogenic tumors are classified as:

1. Adenocarcinoma.
2. Squamous cell carcinoma.
3. Carcinoma of type undetermined.
4. Indifferent basal cell carcinoma.

GRADING

Bronchogenic tumors must be graded with caution. The grading of tumors generally is well accepted, and the scheme of Broders can be carried out successfully by experienced pathologists upon the tissue alone in many tumors. In the study of biopsy material from bronchogenic tumors, the fragment is by necessity small and represents often only a very small part of the tumor. It has been our experience that several specimens taken at various intervals have shown different degrees of malignancy as this is determined by cytologic structure. Let it not be understood that we in any way, because of the smallness of the fragment or the small proportion of the tumor it might represent, or even the inability to obtain tumor tissue in some 30 per cent of cases, believe that biopsy is not of proved value. On the contrary our cases have demonstrated its necessity. For example, two patients came to us with a previously made diagnosis of foreign body (and foreign body was found), but fragments of the "inflammatory" tissue revealed the presence of carcinoma. Tuberculosis and nonspecific inflammations likewise have been accompanied by grossly unrecognizable carcinoma that was only revealed by biopsy. We venture to say that carcinoma might have been missed until a later date had not the biopsy material been examined. We believe that at least in this field of study the older method of grading is likely to be more accurate; wherein the degree of dissemination of the tumor and the rapidity of growth as well as the clinical evidence of metastasis, facts learned by clinical study and roentgenography, should temper the opinion formed by the investigation microscopically of removed tissue. Biopsy comprises but one, yet a necessary point in the diagnosis of bronchopulmonary disease.

CASE REPORTS

In the series of cases briefly reported herewith, the bronchoscopies were done either by Dr. Chevalier Jackson or by Dr. Chevalier L. Jackson. In each instance the bronchoscopist is indicated by the initials "C. J." or "C. L. J."

CASE 1.—*History:* A. A., a tailor sixty-two years of age, complained of a "dry hacking cough" for the past year. Some expectoration of "bloody mucus." "Soreness in chest" but no definite pain.

X-ray Examination: "Bronchial carcinoma, probably arising from right lower lobe bronchus. There are diffuse metastases throughout both lung fields and a metastatic lesion destroying a large portion of the right first rib." (Merchant.)

Bronchoscopy (C. J.): After removal of a smooth polypoid mass of exudate there was seen intruding inward from the anterior wall of the middle lobe bronchus a semiglobular mass, pinkish yellow in color, that crowded the thickened dividing spur and the subjacent wall backward. Pus aspirated and specimen taken for biopsy.

Biopsy: Metastatic carcinoma of "clear cell" type (hypernephroma?).

CASE 2.—*History:* W. A., a physician thirty-nine years of age, complained of a productive cough for five and one-half months, but said he had "had chronic bronchitis for many years." Some pain noted also, and hemoptysis.

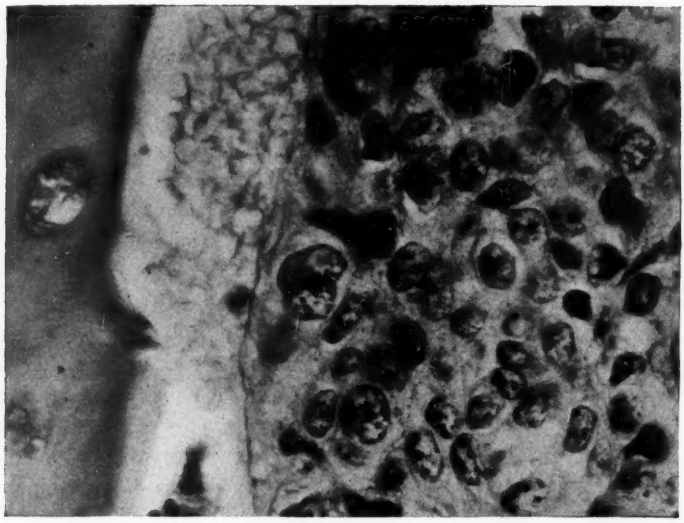


Fig. 1.—(Case 2.) Squamous cell carcinoma (Class B). Grade III. An area showing marked pleomorphism. The cell mass is invading the bronchial cartilage seen on the left. T. U. H. Lab. No. 14,161. (675×.)

X-ray Examination: First examination: "Pulmonary tuberculosis with small cavities in right upper and middle lobe." Second examination, about one month later: "In the presence of such a high degree of atelectasis associated with a completely drowned right lung, the possibility of a bronchial carcinoma at the right hilum must be borne in mind." (Chamberlain and Merchant.)

Bronchoscopy (C. J.): Middle lobe orifice found distorted and almost closed. Right lower lobe bronchus completely obstructed by firm tissue, somewhat ridged, the ridges extending downward to the right and ending in an obliterated lumen. Pus aspirated and specimen of tissue taken for histologic examination.

Biopsy Report: Squamous cell carcinoma, Grade III. (Class B.) Fig. 1.

CASE 3.—*History:* M. A., a woman clerk thirty-one years of age, complained of a slight cough with a small amount of expectoration, which she dated from a "cold" five months previously. She had had some hemoptysis but no pain.

X-ray Examination: Partial atelectasis of left lung, with some displacement of mediastinal structures to left. (At one time films showed pleural effusion with displacement of mediastinal structures to the right, but after thoracentesis displacement to the left was again noted.) (Merchant.)

Bronchoscopy (C. L. J.): In the left bronchus, at about the point at which the left upper lobe bronchus is given off, a rounded, gray white tumor mass was found, almost completely occluding the lumen. Scanty amount of secretions present. Specimen taken for biopsy.

Biopsy: Carcinoma of indifferent type, Grade IV. (Class F.)

CASE 4.—*History:* J. A., a physician fifty-three years of age, complained of productive cough, with blood-streaking, for four or five months.

X-ray Examination: "Large lesion involving the apex of the right lower lobe, probably bronchial carcinoma." (Pancoast.)

Bronchoscopy (C. J.): Right bronchus found almost completely filled by grayish yellow nodular masses springing from a bloody ulcerated bed.

Biopsy: Adenocarcinoma, Grade III. (Class A.)

CASE 5.—*History:* L. M. B., a clerk fifty-two years of age, complained of productive cough as long as he could remember, worse in past four or five months. Syphilis contracted at age of twenty-six, but had been treated; Kahn test now 3-plus.

X-ray Examination: "Atelectatic right lower lobe, probably due to bronchial carcinoma, but inflammatory disease of lymph glands of mediastinum thought a possible diagnosis." (Young.)

Bronchoscopy (C. J.): Yellowish mound found projecting into lumen of right lower lobe bronchus. Pus aspirated and specimen taken for biopsy.

Biopsy: Carcinoma of indifferent type, Grade IV. (Class E.)

CASE 6.—*History:* P. B., a clerk forty-two years of age, complained of slight hemoptysis and slight intermittent pain in the chest. Had influenza six years before, and two attacks of "pleurisy," both right-sided, within past year.

X-ray Examination: "The condition in the right lung root and in the lung just in front of the lung root seems very definitely to be a neoplasm, but bronchial carcinoma does not explain the appearance in all of its details. In the first place, it would be unusual for a bronchial carcinoma to reach this size without completely shutting off some parts of the right lung, with consequent complete atelectasis. In the second place, there are certain other neoplasms which have a greater tendency to extend along the interlobar septum in the way that this has." (Chamberlain.)

Bronchoscopy (C. J.): Small tumorlike mass found attached to the distal margin of the right upper lobe bronchial orifice. External wall of subjacent bronchus crowded inward.

Biopsy: Adenocarcinoma, Grade II. (Class A.) Figs. 2 and 3.

CASE 7.—*History:* R. P. B., a banker fifty-five years of age, complained of productive cough with profuse expectoration for the past seven months.

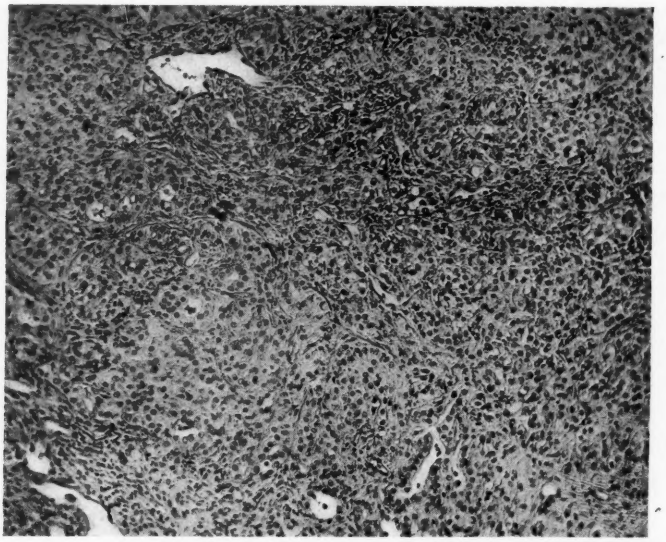


Fig. 2.—(Case 6.) Adenocarcinoma, Grade II. Note the rather typical acinar arrangement of cells. T. U. H. Lab. No. 9669. (150×.)

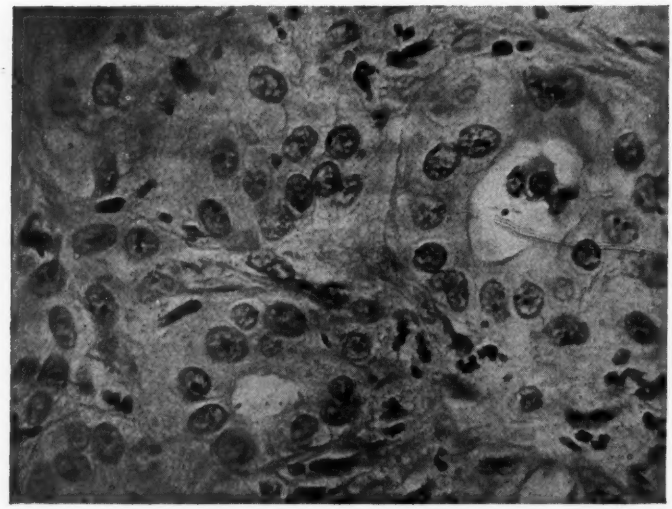


Fig. 3.—(Case 6.) Adenocarinoma, Grade II. Higher magnification of Fig. 2. (600×.) Compare with Fig. 4.

X-ray Examination: "The x-ray appearance at the present time and in all of the previous films is characteristic of primary bronchial carcinoma arising at or

very close to the right hilum, and extending mostly into the right upper lobe but to some extent into the right lower lobe. It is possible that the middle lobe has been spared.'' (Chamberlain.)

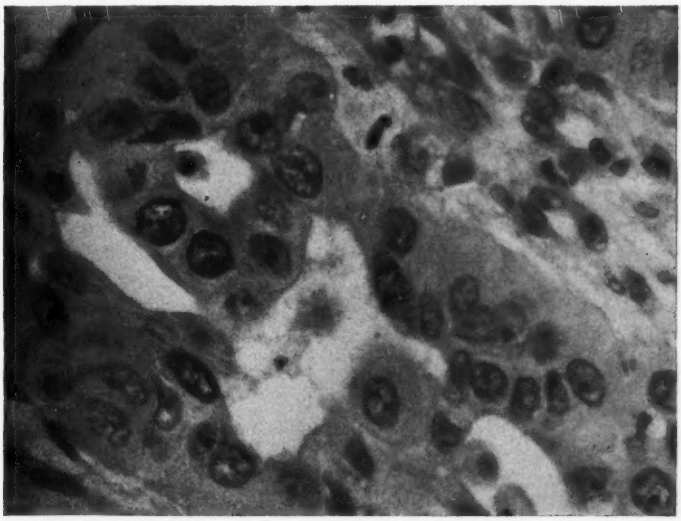
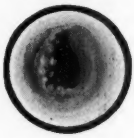


Fig. 4.—(Case 8.) Carcinoma of "combined" type. Note the suggestive glandular structure by cuboidal cells. Compare with Fig. 3. T.U. H. Lab. No. 14,679. (650×.)

Fig. 5.—(Case 8.) The area shown is not far distant from that in Fig. 4. Observe the squamous keratin-producing cells and in the encircled area intercellular spines are in focus. T. U. H. Lab. No. 14,679. (650×.)

Bronchoscopy (C. J.): Dec. 23, 1932. Rigidity and deformity of the right bronchus noted, with some widening of the carina, but no endobronchial tissue suitable for biopsy seen. Diagnosis of peribronchial malignant growth made and roentgen therapy advised.

April 18, 1933. Right bronchus still more crowded-in and occluded. Mucosa of median wall now nodular and bleeding. Specimen taken for histologic examination.



Biopsy: Adenocarcinoma, Grade III. (Class A.)

CASE 8.—*History:* A. B., a shoe cutter fifty-three years of age, complained of a productive cough which he claimed to have had for twelve years. About five

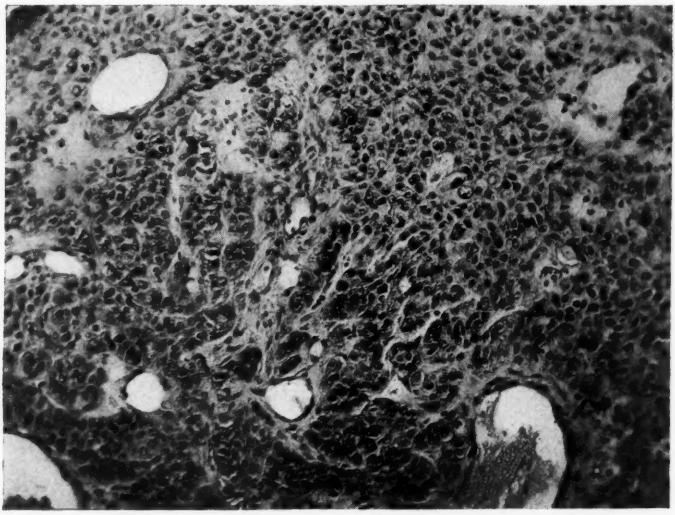


Fig. 6.—(Case 9.) Carcinoma, type not determined (Class C), Grade III. The cells are densely packed. Nothing characteristic of either squamous cells or gland cells can be distinguished. T. U. H. Lab. No. 12,667.

months previous to admission he had had a rather prolonged hemoptysis (nine weeks) but there had been none since that time. Pain in left side of chest and back, dyspnea on exertion, and a loss of about twenty-two pounds in weight were other complaints. (A previous diagnosis of tuberculosis had been made, and the patient had spent some time in a sanatorium, from which institution he was referred to us.)

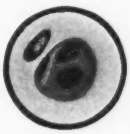
X-ray Examination: Extensive disease of the left lung with hydropneumothorax, interpreted as a tuberculous process.

Bronchoscopy (C. L. J.): In the left bronchus there was some fungating, bleeding tissue which bled readily on contact with the tube. Specimens of secretions and tissue taken for study in the laboratory.

Biopsy: Carcinoma of "combined" type, Grade III. (Class D.) Figs. 4 and 5.

CASE 9.—*History:* J. B., a sheet metal worker forty-seven years of age, complained chiefly of pain, six or seven months in duration.

X-ray Examination: "Thickened pleura, entire left chest, with displacement of the heart and other mediastinal contents to the left." (The appearances were really those of atelectasis of the left upper lobe.)



Bronchoscopy (C. L. J.): Just inside the orifice of the left upper lobe bronchus there was found a fungation which was removed for biopsy. (See Plate I also.)

Biopsy: Carcinoma, type undetermined, Grade III. (Class C.) Fig. 6.

CASE 10.—*History:* T. F., a housewife thirty-five years of age, complained chiefly of pain in the chest, but also of slight dysphagia. No cough or hemoptysis.

X-ray Examination: "Study of the esophagus showed a slight obstruction to the passage of the opaque mixture in the midthoracic esophagus, but it also showed a lesion in the apex of the right lower lobe which 'strongly suggested' primary bronchial carcinoma." (Pancoast.)

Bronchoscopy (C. L. J.): The lumen of the right stem bronchus was found markedly narrowed by the encroachment of its median wall, preventing full exposure of the middle lobe bronchus. This bulging median wall seemed infiltrated, and a specimen was taken from it for biopsy. (See Plate I also.)

Biopsy: Carcinoma of indifferent type. (Class F.)

CASE 11.—*History:* A. F., a carpenter forty-six years of age, was sent to us from a sanatorium where all tests for tuberculosis had been negative. He complained of slight pain of about ten weeks' duration, and slight cough, with blood-streaked sputum. He had lost thirty pounds in weight in ten weeks.

X-ray Examination: March 21, 1931. "Abscess of the right upper lobe with definite evidence of cavity formation but no fluid level."

April 21. "Slight improvement" thought to have occurred.

May 6. "Heavy homogeneous density completely filling right upper lobe, which is definitely shrunken, probably atelectatic." Diagnosis of bronchial carcinoma made. (Young.)

Bronchoscopy (C. L. J.): Orifice of right main bronchus involved in a bleeding ulcerated lesion which seemed to block almost completely the orifice of the right upper lobe bronchus. Specimens of secretions and tissue taken for laboratory examination. (See Plate I also.)

Biopsy: Squamous cell carcinoma, Grade III. (Class B.)

CASE 12.—*History:* W. H. F., a retired business man sixty-three years of age, complained of a "tight feeling" in the chest for seven months; also a slightly productive cough. He had lost seven or eight pounds in weight. The only item of interest in his past history was the fact that he had had influenza five or six years previously.

X-ray Examination: "Atelectasis of right lower lobe, most likely due to neoplasm of right lower lobe bronchus." (No evidence of metastatic involvement of ribs or spine.) (Merchant.)

Bronchoscopy (C. J.): Right bronchus found completely occluded by a nodular bleeding mass having the appearance and feel of the hard nodular type of carcinoma.

Biopsy: Carcinoma of indifferent type, Grade III. (Class E.) Fig. 7.

CASE 13.—*History:* A. G., miner and laborer forty-five years of age, complained of pain in the chest radiating to the back, and productive cough of about two and one-half months' duration.

X-ray Examination: "Emphysema and pneumoconiosis (late first or early second stage). Right diaphragm high and an area of increased density in right

Fig. 7.—(Case 12.) Carcinoma of indifferent cell type (Class E), Grade III. The small round cells are densely packed. There is little intercellular stroma. T. U. H. Lab. No. 12,651. (150×.)

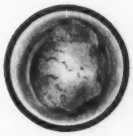
lower lobe adjacent to cardiac silhouette which suggests localized atelectasis, possibly due to bronchogenic carcinoma." (Alexander.)

Bronchoscopy (C. L. J.): Right lower lobe bronchus found narrowed and its lumen distorted. There was marked infiltration of the bronchial walls and some tissue projecting into the lumen. Specimen taken for biopsy. (See Plate I also.)

Biopsy: Adenocarcinoma, Grade III. (Class A.)

CASE 14.—*History:* A. G., a salesman fifty-three years of age, complained of productive cough of many years' duration; in fact he said he had "coughed all his life." There had been slight blood-streaking of sputum in the past year and a half.

X-ray Examination: Sharply circumscribed collection of exudate in lower half of right chest "suggesting interlobar empyema rather than lung abscess." (Manges.)



Bronchoscopy (C. J.): Right inferior lobe bronchus occluded by tumorlike mass of tissue apparently attached by a pedicle. Tissue removed for histologic examination.

Biopsy: Squamous cell carcinoma, Grade III. (Class B.)

CASE 15.—*History:* M. G., a woman thirty-four years of age, complained of slight cough of several months' duration, and rather severe pain in the left chest. Previous diagnoses that had been made were: grip, pneumonia, pleural effusion, and tuberculosis. The chest had been tapped but no fluid obtained.

X-ray Examination: "Findings elsewhere have led to a diagnosis of tuberculous pleurisy on the left side, with effusion. The three masses of density in the upper portion of the left chest are difficult to interpret. My impression is that they are metastatic nodules." (Merchant.)

Bronchoscopy (C. L. J.): Irregular mass of tissue found blocking orifice of left lower lobe bronchus. Specimens of secretions and tissue taken for laboratory study. (See Plate I also.)

Biopsy: Carcinoma of "combined" type, Grade IV. (Class D.)

CASE 16.—*History:* H. H., an automobile dealer forty-three years of age, complained of dyspnea on exertion for the past six months, and pain in the right side of the chest and back. He also noticed some wheezing, and in the past week his sputum was slightly pinkish in color.

X-ray Examination: Films taken two months previously thought negative so far as the lungs were concerned. Recent fluoroscopic study, however, suggested obstruction of the right bronchus, because of restricted motion of the right diaphragm. (Lewis.)

Bronchoscopy (C. J.): Right bronchus found closed by a bulging inward of three masses that came almost together in the midline, leaving a triangular lumen. On advancing the tube beyond this point, a bleeding but very firm mass was found crowding in from the median wall. The bronchus seemed quite rigidly fixed.

Biopsy: Carcinoma, type undetermined, Grade III. (Class C.)

CASE 17.—*History:* J. H., a plumber sixty-one years of age, complained of pain in the abdomen and back for two months, and a loss of thirty-two pounds in weight in six months.

X-ray Examination: Left upper lobe atelectasis, "attributed to a malignant neoplasm, presumably carcinoma of the left upper bronchus." (Merchant.)

Bronchoscopy (C. L. J.): Marked bulging of the median wall of the left main bronchus noted just below bifurcation. The bronchial mucosa was infiltrated at this point and the scope was passed beyond with some resistance. Specimens taken for histologic examination. (See Plate I also.)

Biopsy: Carcinoma, type undetermined, Grade III. (Class C.) Fig. 8.

CASE 18.—*History:* J. K., a butcher fifty-six years of age, complained of painful cough of one month's duration. He gave a history of an operation for removal of a tumor of the left kidney ("hypernephroma") two years previously.

X-ray Examination: "Right diaphragm very high, due to atelectasis of right lower lobe caused by bronchial obstruction, probably foreign body or tumor." (Young.)

Bronchoscopy (C. L. J.): Right stem bronchus found almost completely filled by an irregular bleeding mass covered with a grayish exudate. Several specimens of tissue removed for biopsy. (See Plate I also.)

Biopsy: Metastatic carcinoma of "clear cell" type (hypernephroma?).

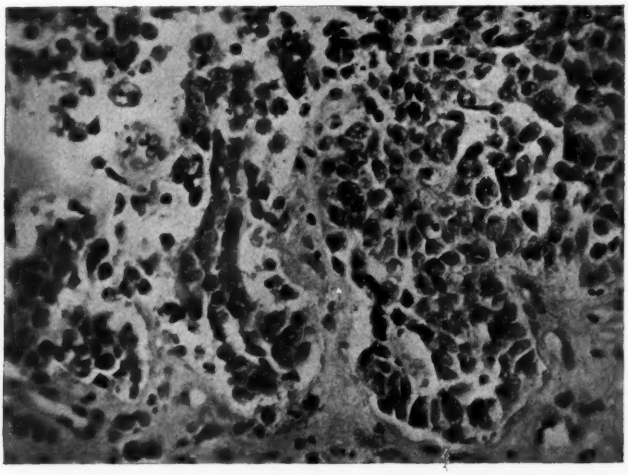
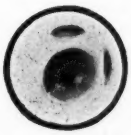


Fig. 8.—(Case 17.) Carcinoma in which type could not be determined (Class C), Grade III. Much of the tissue appears as in Fig. 6, but one area revealed the structure seen in the photograph. The cells in the area shown behave as "basal" cells. T. U. H. Lab. No. 11,487.

CASE 19.—*History:* M. K., a laborer forty-eight years of age, complained of a productive cough for about six months prior to admission. He had also had some loss of weight and some chills and night sweats.

X-ray Examination: A series of roentgen ray studies was made, but "chronic suppurative pneumonitis" was the diagnosis that seemed most probable from the roentgenologist's point of view.

Bronchoscopy (C. L. J.): Right lower lobe bronchus found partially obstructed by an irregular, nodular, proliferative lesion, from which specimens of tissue were removed. A considerable amount of mucopurulent secretion was present. (See Plate I also.)



Biopsy: Carcinoma of indifferent type, Grade III. (Class E.)

CASE 20.—*History:* F. H. K., a carpenter forty-four years of age, complained of productive cough of fifteen years' duration. He had lost forty pounds in six months.

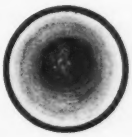
X-ray Examination: "Right lower lobe atelectatic and shrunken to approximately one-fifth of its former size. The carnified right lower lobe is the seat of a chronic pneumonic process."

Bronchoscopy (C. L. J.): Middle and right lower lobe bronchi found partially obstructed by irregular masses of tissue which bleed easily on contact with the scope. Moderate amount of secretions present. Specimens taken for biopsy. (See Plate I also.)

Biopsy: Carcinoma, type undetermined, Grade III. (Class C.)

CASE 21.—*History:* F. K., a clerk forty years of age, complained of productive cough of three years' duration, with some blood-streaking in the past three months. He gave a history of tooth extraction (eleven teeth) several months previously, following which symptoms had seemed to be worse.

X-ray Examination: "Dense lesion involving practically all of the right lower lobe, with considerable element of contraction or collapse, because the heart is displaced appreciably to the right." (Manges.)



Bronchoscopy (C. J.): Jan. 28, 1930. Tooth removed from right lower lobe bronchus. (Some improvement followed, but patient was asked to return for further study because of bronchial stenosis.)

June 20, 1930. Tissue removed from stenotic portion of right lower lobe bronchus, and sent to laboratory for histologic study.

Biopsy: Squamous cell carcinoma, Grade III. (Class B.)

CASE 22.—*History:* L. L., a housewife forty-eight years of age, complained of productive cough of about three years' duration. She also had pain in the back and chest, dyspnea on exertion, and a weight loss of about eighteen pounds. (Patient had right breast amputated twelve years previously.)

X-ray Examination: High right diaphragm, possible tumor mass at roots of both lungs; old tuberculosis of both lungs. (Merchant.)

Bronchoscopy (C. L. J.): Several bronchoscopies were done on this patient. The first (Aug. 15, 1932), showed the right lower lobe bronchus filled with bloody secretions and dark reddish tissue, some of which was removed for biopsy but reported "inflammatory." Subsequently (May 23, 1933), after an interval of nine months, we had an opportunity of doing another bronchoscopy. The right stem bronchus was found markedly narrowed, and there was some hyperplastic tissue intruding into the lumen from the posterior wall. The middle lobe bronchus could not be exposed because of the narrowing of the lumen of the stem bronchus. Additional specimens were taken for biopsy.

Biopsy: Carcinoma of indifferent type, Grade IV. (Class E.)

CASE 23.—*History:* G. M., an unemployed clerk sixty-seven years of age, complained of pain in the chest and productive cough for five weeks. He had lost twenty-five pounds in one month.

X-ray Examination: Pneumonic condition in cephalic third of right lower lobe. "Bronchogenic carcinoma must be borne in mind." (Chamberlain.)

Bronchoscopy (C. L. J.): Right lower lobe bronchus found almost occluded with fungating tissue which extended up along the median wall of the bronchus into the stem bronchus. Considerable quantity of pus aspirated on advancing aspirating tube through the stenosis. (See Plate I also.)

Biopsy: Carcinoma of indifferent type, Grade IV. (Class F.)

CASE 24.—*History:* H. M., a dentist fifty-six years of age, complained of a "spasmodic pain" of several years' duration, worse in the past year; also of a moderately productive cough. History of tooth extraction and presence of a suspicious shadow in the films suggested possible foreign body.

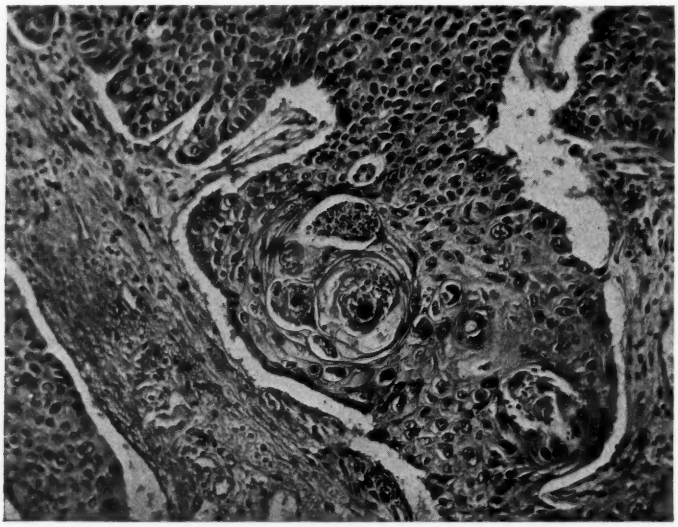


Fig. 9.—(Case 24.) Squamous cell carcinoma (Class B), Grade III. A typical picture of this variety of tumor. T. U. H. Lab. No. 11,117. (150×.)

X-ray Examination: "Almost complete atelectasis of left lower lobe; soft tissue mass just above the left main bronchus, due to inflammatory change in lymph glands. Small dense shadow noted at apex of triangular or pyramidal shadow of atelectatic left lower lobe." (Chamberlain.)

Bronchoscopy (C. J.): Several bronchoscopies were done, and the small dense object seen in the films was removed under biplane fluoroscopic guidance. It proved to be a broncholith. Subsequently suspicious tissue was removed for histologic examination.

Biopsy: Squamous cell carcinoma, Grade III. (Class B.) Fig. 9.

CASE 25.—*History:* D. M., a salesman fifty-two years of age, complained of productive cough dating from "tonsillitis" eight months previously. He also had some dyspnea and had lost twenty pounds in weight.

X-ray Examination: "Area of density occupying roughly the area of the middle lobe. Right diaphragm slightly elevated." (Stull.)

Bronchoscopy (C. J.): Internal wall of right main bronchus crowded to the right at the bifurcation. Continuous with this, the median wall encroached upon the lumen of the bronchus all the way down to the orifice of the middle lobe bronchus, which seemed closed. Mucosa intensely red and bleeding; somewhat granular on the surface.

Biopsy: Carcinoma, type undetermined, Grade III. (Class C.)

CASE 26.—*History:* J. F. M., a clerk fifty-five years of age, complained of a slight cough with occasional slight blood-streaking. Weight loss was twenty-one pounds in six weeks. Some dyspnea.

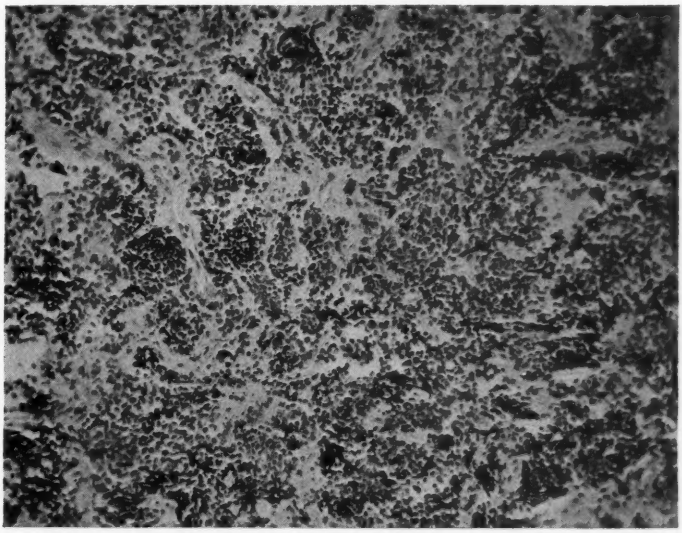


Fig. 10.—(Case 26.) Carcinoma of "indifferent" cell type (Class F). The cells individually are much like those seen in Fig. 7. Yet there is more of an attempt to line spaces or form cords or tubes. T. U. H. Lab. No. 13,483. (150×.)

X-ray Examination: "Entire left chest opaque, heart and great vessels displaced to the left, suggesting atelectasis due to tumor as the most likely diagnosis." (Pancoast.)

Bronchoscopy (C. L. J.): Large mass found obstructing the left main bronchus. Specimen taken for biopsy. (See Plate I also.)

Biopsy: Carcinoma of indifferent type, Grade IV. (Class F.) Fig. 10.

CASE 27.—*History:* L. N., a shoemaker forty-three years of age, complained of a productive cough and persistent pain in the chest of seven months' duration. He also noted some dyspnea and slight dysphagia. (History of "flu" in 1918.)

X-ray Examination: Atelectasis of right lower lobe, with displacement of heart and mediastinal structures to the right. "Bronchial malignancy" suggested. (Episcopal Hospital.)

Bronchoscopy (C. L. J.): Right bronchus found very much stenosed anteroposteriorly. The mucous membrane was puckered, and bloody secretions were oozing up from below.

Biopsy: Squamous cell carcinoma, Grade III. (Class B.)

CASE 28.—*History:* A. O., a salesgirl twenty years of age, consulted a physician because of inability to walk due to "weakness of the ankles." She also complained of a dull aching pain between the shoulders. On questioning, she admitted a slightly productive cough of two years' duration, with some blood-streaking of the sputum.

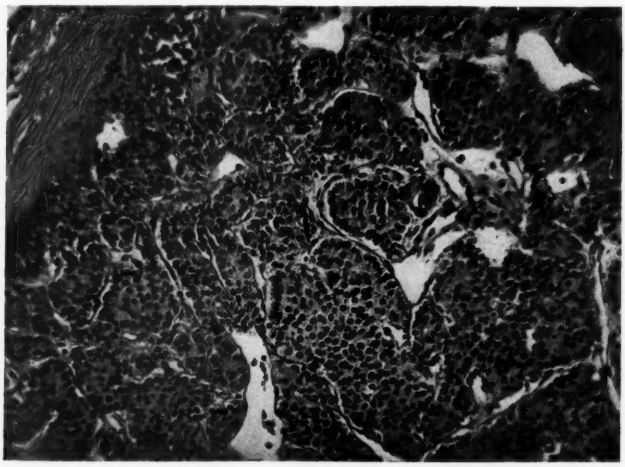


Fig. 11.—(Case 28.) Carcinoma type not determined (Class C), Grade III. The cells are arranged in alveoli, but nothing characteristic of squamous cells or gland cells can be seen. T. U. H. Lab. No. 11,799. (150×.)

X-ray Examination: "Atelectasis of entire left lung, erosion of several ribs in the left upper dorsal region, and changes in the third dorsal vertebra suggestive of metastatic carcinoma." (Chamberlain.)

Bronchoscopy (C. L. J.): Left bronchus found obstructed by irregular soft fungations, and a large quantity of blood-stained mucopurulent secretions coming up from the lower lobe bronchus. (See Plate I also.)

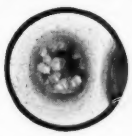


Fig. 11.

Biopsy: Carcinoma, type undetermined, Grade III. (Class C.)

CASE 29.—*History:* J. R., a physician's secretary thirty-nine years of age, complained of paroxysmal attacks of coughing, and was sent in for bronchoscopy because roentgen ray examination had shown an obstructive emphysema of the right lung, and a diagnosis of "bronchial obstruction, probably due to non-opaque foreign body" had been made. Another previous diagnosis was "pulmonary tuberculosis." (Small polyp reported "spindle cell sarcoma" had been removed from uterus seven or eight years before.)

X-ray Examination: Films made on inspiration and expiration indicated the presence of bronchial obstruction (right bronchus) causing obstructive emphysema

of right lung, but mediastinal or bronchial tumors were thought more probable than foreign body. (Merchant.)

Bronchoscopy (C. J.): Carina flattened from before backward; broadened anteriorly but thin posteriorly. In the right bronchus there was a pedunculated growth attached to the anterior wall. On inspiration secretion passed inward; but only occasionally did any bubble out on expiration.

Biopsy: Carcinoma of indifferent type, Grade IV. (Class F.) Fig. 12.

CASE 30.—*History:* C. S., a furniture-finisher fifty-one years of age, complained of a productive cough of ten months' duration, with some blood-streaking. He also

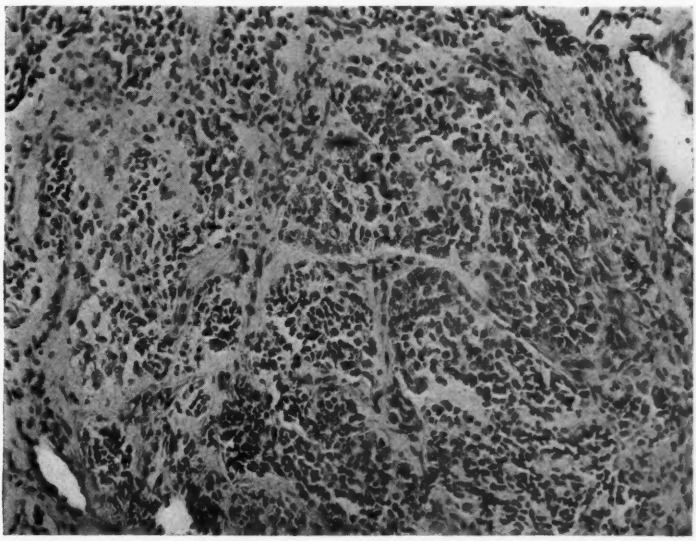


Fig. 12.—(Case 29.) Carcinoma indifferent cell type (Class F), Grade IV. As in Fig. 10, the cells possess but little cytoplasm and round vesicular nuclei. They are loosely scattered in a scant stroma yet a tendency to form cords or tubes is noticeable. T. U. H. Lab. No. 10,535. (120×.)

had severe pain and had lost nineteen pounds in weight. The diagnosis on admission was "pulmonary abscess."

X-ray Examination: "Area of density slightly above and lateral to the left lung-root, in the cephalic portion of which there is an area of radiolucency bounded below by a fluid level. The left lateral projection definitely localizes this in the lower portion of the left upper lobe. Above this area one finds numerous discrete round opacities measuring about 1 cm. in diameter." (Merchant.)

Bronchoscopy (C. L. J.): Orifice of left upper lobe bronchus carefully inspected, and at a depth of about half a centimeter several nodular projections of tissue were seen, from which tissue was taken for biopsy.

Biopsy: Carcinoma, type undetermined, Grade III. (Class C.)

CASE 31.—*History:* C. V., a physician fifty-eight years of age, suddenly experienced a hemoptysis. He had thought himself perfectly well, but had had an in-

termittent dry, irritating cough. He was gaining weight, in fact had gained twelve pounds in a month and a half.

X-ray Examination: Right lower lobe completely atelectatic, but this condition was difficult to recognize because the shadow of the shrunken atelectatic lobe was obscured by the heart shadow. (Merchant and Chamberlain.)

Bronchoscopy (C. J.): Tiny stream of blood followed down to its source, which was found to be in the right lower lobe bronchus, where blood was found oozing up around an occluding tumor mass. Bronchial wall rigid and deformed in outline; middle lobe orifice crowded outward to the right, and its spur deformed.

Biopsy: Squamous cell carcinoma, Grade III. (Class B.)

CASE 32.—*History:* G. W., a housewife thirty-two years of age, complained of a dry, hacking cough of four months' duration, also some pain in the right chest. She gave a history of having had radium treatment for cancer of the cervix nine months previously.

X-ray Examination: Large mass of soft tissue density in the right lung occupying the area of the middle lobe. Limitation of movement of the right leaf of the diaphragm noted on fluoroscopy. Findings thought to indicate partial occlusion of right upper and lower lobes with complete occlusion and atelectasis of middle lobe. (Merchant.)

Bronchoscopy (C. L. J.): Fungating neoplasm found projecting from the middle lobe bronchial orifice and middle lobe spur greatly thickened, causing partial obstruction of lower lobe bronchus. Ample specimens taken for biopsy.

Biopsy: Metastatic (?) carcinoma.

CONCLUSIONS

1. Bronchoscopic biopsy will be positive in about 75 per cent of the cases of bronchial carcinoma.

2. Many of the cases in which biopsy is not possible at the first bronchoscopy will later show endobronchial intrusion; though the surgeon should not wait for this if consent is given for exploratory thoracotomy.

3. Even in cases where biopsy is *not* possible, bronchoscopic findings may be of definite diagnostic value.

4. A simple classification of bronchogenic carcinoma that can be understood and followed by pathologist, bronchoscopist, and radiologist is desirable.

5. Microscopic evidence of malignancy does not imply necessarily an extensive infiltrative tumor, and therefore the grading of bronchogenic carcinomas should be tempered by a knowledge of the bronchoscopic and roentgenographic findings.

6. Biopsy studies are of great value, yet constitute but one of the important considerations in the diagnosis of bronchogenic tumors. Teamwork by the bronchoscopist, radiologist, and pathologist will accomplish a proper prognosis and guide the patient to the most beneficial form of treatment.

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DISCUSSION ON "MALIGNANT DISEASE OF THE LUNG," BY MR. EDWARDS; "BRONCHIOGENIC CARCINOMA: A CLASSIFICATION IN RELATION TO TREATMENT AND PROGNOSIS," BY DRS. TUTTLE AND WOMACK; "A TOPOGRAPHIC CLASSIFICATION OF PRIMARY CANCER OF THE LUNG—ITS APPLICATION TO THE OPERATIVE INDICATION AND TREATMENT," BY DRS. RABIN AND NEUHOF; "BRONCHIAL CARCINOMA; BRONCHOSCOPIC BIOPSY IN A SERIES OF 32 CASES," BY DRS. JACKSON AND KONZELMANN.

DR. RICHARD H. OVERHOLT.—I should like to take a moment to discuss the successful removal of the lung (pneumonectomy) for malignancy in two cases.

CASE 1. A woman thirty-three years of age (Mrs. A. T.) was first seen in October, five months after the onset of respiratory symptoms. An x-ray picture of the chest showed a discrete shadow in the right lung near the hilum. There was haziness below, indicating atelectasis of the right lower lobe. Bronchoscopy revealed a mass in the right lower main bronchus which occluded its lumen. Biopsy was negative for neoplasm. Regardless of this fact, however, a diagnosis of primary carcinoma of the lung was made from the history, x-ray and bronchoscopic evidence, of an occluding lesion in the bronchus. Pneumothorax was instituted and maintained for ten days prior to operation. A right total pneumonectomy was performed on November 13, 1933. Cyclopropane anesthesia was used. An anterolateral incision was made. Tourniquets were used on the hilum. The stump was closed with silk ligatures. The wound was closed without drainage. Convalescence was uneventful except for the development of a thoracic sinus which closed after a two-stage thoracoplasty had been completed. The thoracoplasty operations were done on January 12 and February 26, 1934. The patient is now symptom free, able to do part of her housework and seems to be in comparatively good health.

Histologic examination showed the lesion to be a bronchiogenic carcinoma.

CASE 2. A woman forty-two years of age (Mrs. E. H.) was seen in April, 1934, five months after the onset of symptoms. An x-ray picture of the chest showed atelectasis of the left lower lobe and obstructive emphysema of the upper lobe. Upon bronchoscopic examination, a tumor was found in the left lower bronchus which partially occluded the left upper bronchus. A biopsy was taken and a carcinoma found. There were no demonstrable evidences of metastasis. The patient was prepared by providing a pneumothorax on the involved side for twenty-one days before operation. A left total pneumonectomy was done on May 2. A posterolateral incision was made. The stump was treated similarly to the method used in the first case. Examination of the removed lung suggested that the lesion had been completely excised. Lymph glands on the removed specimen did now show metastasis. The wound was closed without drainage. Convalescence has been uneventful. At regular intervals fluid has been withdrawn from the chest and air replaced to maintain a physiologic intrapleural pressure. The fluid has remained sterile. The wound is healed firmly. A fistula has not developed. The patient is still in the hospital and is free of symptoms except for a sense of pressure in the left chest. A decision regarding the necessity of thoracoplasty has not been made.

I might add a word about the anesthesia used. Both cases were operated upon under cyclopropane intratracheal anesthesia. The apnea technic was used. After the thoracic cage was opened, the anesthetist increased the percentage of oxygen, stopped respiratory movements entirely and held the patients under complete apnea throughout the period of time necessary to do the intrathoracic work. After the lung had been removed and the stump closed, movements of respiration were then started by running carbon dioxide into the circuit. Respiration was then resumed while the wound was being closed.

I might also add that in dealing with suspected cases of primary carcinoma of the lung, we feel it is advisable to do complete gastrointestinal x-ray series and also to examine the spine, ribs and long bones by x-ray to make sure there are no metastases.

(Lantern slides illustrating the cases were shown.)

DR. HARRY R. DECKER.—I should like first to pay tribute to Mr. Edwards' paper. It is stimulating to men in this work who have not had wide experience to receive the fine reports of his success, and such reports as Dr. Graham, Dr. Overholt, Dr. Eggers and Dr. Churchill have given us of the successful removal of malignancy of the lung.

The question that I am rising to speak about is—when is a carcinoma not a carcinoma? We know, of course, as Dr. Neuhof suggested in his paper, that if the tissue is removed, particularly by bronchoscopy, it is carcinoma. Yet, some of these patients go on to recovery clinically and do not die.

I have had, in the last two or three years, under observation in connection with my colleague, Dr. Marcy, three cases in which a competent pathologist returned to us on the basis of specimens submitted, diagnosis of carcinoma. At the time that these patients were bronchoscoped the bronchoscopist assured us that the patients definitely had grossly malignant tumors. They had the appearance of being submucosal, being sessile in type, not pedunculated, and not having the aspects of benign polyp or adenoma. No attempt was made other than to obtain the specimen for biopsy. No effort was made to remove the tumors in toto, although in one case the whole tumor was removed.

Those three patients have been followed carefully for three years, and they are clinically well. Yet our pathologist assured us that the specimens, on the basis of microscopic study, on account of the appearance of the tumor cells, the mitoses, vascularity and by whatever tests a competent pathologist makes, were malignant tumors. In one case, he had a definite notion that it was a typical anaplastic carcinoma that he was reporting.

It is hard for me to understand the clinical situation on that basis, and it certainly puzzles the surgeon to know what to do under the circumstances. Should those patients be treated with radium at first; should one wait until a recurrence of the growth takes place and then do a radical procedure; or should one, under the circumstances, at once do a lobectomy or a pneumonectomy, as the case may be?

Dr. Broecker, the pathologist I referred to, offers a suggestion which is, I think, somewhat speculative, yet it may be of some interest: that these cases may represent herniation of alveolar tissue through the bronchus, at a given point. These three patients had a history of acute respiratory disease of a protracted nature. He suggests this because in many cases of unresolved pneumonia that he has had to deal with, there has been a confusing picture which has been suggestive of malignancy.

DR. EDWARD W. ARCHIBALD.—I share Dr. Decker's confusion of mind and perhaps can contribute somewhat to that confusion.

To judge from Dr. Neuhof's and Dr. Graham's papers, it would appear that our knowledge of pathology needs greater precision. As far as I could see, Dr. Neuhof's basis for prognosis was diametrically opposed to that of Dr. Graham. We have obviously to await further work.

May I mention one confusing thing in regard to pathologic diagnosis which occurred in our hospital. A bronchoscopic biopsy brought forth a piece of tissue which was diagnosed by the pathologist, at McGill, as carcinoma. The lung was removed and the tumor was then pronounced to be sarcoma. Moreover, the tumor was apparently not connected at all with the stem bronchus from which the original piece of tissue had been taken, and the stem bronchus itself was found free of disease. The pathologist professed himself unable to explain the difference in diagnosis. Possibly the explanation offered by Dr. Decker's friend might apply.

May I say a word or two concerning Mr. Edwards' paper, with particular regard to one point. I refer to the assumed safety of exploratory thoracotomy. I have done several of these, and have found the operation not entirely devoid of danger, nor does it always yield the information desired. In one patient with infection of the lobe behind the carcinoma, as determined by palpation, an embolism of the left femoral artery was observed the next day. It led to gas gangrene, amputation, and death. There is, therefore, some danger, I think, of dislodging thrombi from an infected lung by palpation.

Exploratory thoracotomy is also not always informative. One feels as far as one can around the mediastinum for metastases in glands; but if, as is frequently the case, stagnation distal to the tumor has brought on an infective condition of the lung, there will often have developed such massive adhesions in the spinal gutter behind, that the mediastinal structures are entirely obscured. One feels only a diffuse thickening which may be inflammatory but which may also, as in one instance in which I attempted eradication of the lung, represent in reality an extension of the carcinoma under the pleura and up the mediastinum.

One word about the line of approach. Mr. Edwards posed the question whether the anterior approach might not be the better. Overholt has told us he opened anteriorly in his first patient and posteriorly in the second. He does not indicate which he found the better.

For my own part, I might recall to you that two years ago at Ann Arbor I reported briefly my first total pneumonectomy operated on in November or December of 1931. Beginning the operation behind and finding very dense adhesions, I was unable to do more than resect the lower lobe, which was infected. One or two months later I removed the upper lobe with the stem bronchus through an anterior incision and found that approach quite easy. If the hilar tissues are not seriously thickened by inflammation or by cancer, the anterior approach allows one to dissect easily and ligate the vessels, thus controlling the circulation as a desirable first step, and then to go deeper and secure the main bronchus. This is true only of the left side. On the right side, this procedure is anatomically much more difficult. I have since done a second left total pneumonectomy in one stage with good operative success, with no disturbance of the physiologic balance, and technically with comparative ease. Dr. Rienhoff, in Baltimore, has also used this approach twice with great satisfaction.

I have referred to anatomical difficulties on the right side. Here the pulmonary artery and vein divide almost immediately into three or four branches instead of one or two, as on the left side; and the right stem bronchus divides also quickly into the eparterial, the middle, and the lower, so that one finds it necessary to tie a half dozen or more vessels and bronchi instead of two or three. Not only that but the right lung covers the edge of the heart more closely than does the left. The anterior mediastinal approach is therefore more difficult on the right side than on the left. In the inflammatory cases, with thickened mediastinum, I do not see how one can do better than a mass ligation, especially on the right side. I should have been glad if Dr. Overholt had explained the details of his technic of right-sided total pneumonectomy.

DR. HOWARD LILIENTHAL.—Permit me to discuss briefly some points from the splendid papers and demonstrations which you have just heard.

A year or two ago Mr. Nelson allowed me to see the instrument of Mr. Tudor Edwards for the implantation of radium into the lung. There is no doubt that if radium is to be used it should be implanted with accuracy. Unquestionably if carcinoma of the lung is inoperable, the employment of radium is most desirable. As to operability, much depends upon the proximity of the tumor to the trachea.

A case in which suppurative pneumonitis of the lower lobe had occurred as a result of carcinoma of the lower lobe bronchus was successfully operated upon by me and will soon appear in the *American Journal of Surgery*, the patient having been presented at the meeting of the New York Society for Thoracic Surgery. I will say, however, that with a suppurating lower lobe and the accompanying infiltration of its bronchus I was unable to do more than a lobectomy without assuring myself of being beyond the tumor. Subsequent bronchoscopy revealed that I had been successful.

The remarks which Mr. Edwards has made regarding sarcoma of the mediastinum, especially lymphosarcoma, are of importance. It is perfectly true that in some instances x-ray treatment acts beneficially, but I beg you not to forget the amazing results which have been reported after the use of Coley's mixed toxins of erysipelas and prodigiosus. The great advantage of the toxins is that it is a general treatment and not a local one. Besides, the use of the toxins does not forbid x-ray treatment when no favorable progress is apparent. In one of my cases in which an enormous mediastinal tumor had invaded the spine and had produced paraplegia the neoplasm disappeared after biopsy and treatment with Coley's fluid. (Mediastinal Sarcoma—Treated by Coley's Fluid, Ann. Surg. **81**: January, 1925.) Treatment of inoperable sarcoma of any kind by Coley's fluid has been successful in a considerable number of cases in which I have employed it.

The two cases of total pneumonectomy by William F. Rienhoff, Jr., of Johns Hopkins are illuminating in demonstrating what can be done in this apparently hopeless condition. We must note, however, that in both of these cases no suppuration was present.

It is remarkable that at this meeting two classifications of carcinoma should be presented, one by Dr. Graham and the other by Dr. Neuhof. I am fairly well convinced that primary "parenchymatous" carcinoma of the lung can occur, although I admit that metastatic parenchymatous carcinoma is far more common than the primary variety. When a tumor of this kind is encountered, every effort should be made to find the parent growth.

The selection of treatment of any given case of carcinoma of the lung should be decided upon after reviewing all the circumstances of the case.

DR. CARL EGGERS.—The various presentations have shown that there is apparently considerable confusion regarding the pathology of these tumors, particularly those affecting the main bronchi. I have no doubt that individual members of this Society, who may not have a large group to report, have isolated or small groups of cases, the study of which would aid in the clarification of this subject. We have several such cases at the Lenox Hill Hospital. Being primary tumors of the main bronchus, they were treated by the bronchoscopist and treated so successfully that they have resulted in an apparent cure. The pathologic diagnosis in these cases was carcinoma, but the course was so benign and the result of treatment with electrocoagulation or radium so satisfactory that doubt has arisen in our minds whether these growths are really true carcinomas.

One of these cases was of a boy, B. B., twelve years of age, who was referred to me in February, 1931, with the diagnosis of postpneumonic empyema. The physical signs did not agree with this diagnosis, but roentgen ray pictures were interpreted as indicating a pleural effusion. An exploratory puncture yielded a few cubic centimeters of turbid fluid which showed no organisms in the smear and was negative on culture. He ran a septic temperature reaching 103° F. in the evening. There was a persistently high blood count, with W.B.C. 30,000-37,000, and a polymorphonuclear count of 95 or 96 per cent. One of the x-ray pictures showed a shadow in the left main bronchus, very much like those shown by Dr. Overholt. A foreign body was suspected and a bronchoscopy advised, but was refused by the family. There was gradual improvement in the patient's general condition, his temperature came down, and coincident with that there was clearing of the left lung. He was discharged about three weeks after admission, much improved but not well; and we had a feeling that we had not determined the true cause of his symptoms. He was instructed to report from time to time for examination but failed to do so.

About fourteen months later he was readmitted with symptoms and findings similar to those on his first admission. A bronchoscopy was done which revealed a

tumor partially obstructing the left main bronchus. A biopsy specimen was reported "small-celled carcinoma of the bronchus." The tumor was destroyed with the aid of diathermy in several sittings. This resulted in complete relief of symptoms, apparently chiefly because of the fact that free drainage of the bronchial tree was made possible. The patient was kept under observation and was bronchoscoped at intervals in order to detect possible recurrence of the tumor. He gradually developed a stenosis of the bronchus due to scar contraction at the site of the tumor, which necessitated dilatation through the bronchoscope. He managed to get along fairly well, however, until about sixteen months after destruction of his tumor when he had a chill, followed by fever and expectoration. At first pneumonia was diagnosed, but later it became evident that he had a suppurative intrapulmonary focus apparently due to stenosis of the bronchus. He was referred back to the surgical service and was operated on January 31, 1934. A portion of the ninth and tenth ribs was removed, and a pus-soaked lower lobe was entered. There was no bronchial communication. Culture of the pus showed influenza bacilli. Drainage continued profuse. Later there was some communication with the bronchus. Except for an intercurrent scarlet fever, he has slowly improved. What we shall eventually have to do will be determined by his future course. With a closed bronchus it is possible that the suppurative process may gradually destroy the lower lobe and then lead to a cure. If that does not take place, and his general condition warrants it, a lobectomy may become the procedure of choice.

It is now almost two years since the tumor of the bronchus was destroyed, and there has been no sign of recurrence or metastasis. Although the diagnosis of carcinoma was made by Dr. F. D. Bullock of our hospital, who is a very able and careful pathologist, we are in doubt whether we are dealing with a true carcinoma. The opinion has been expressed, as Dr. Overholt mentioned, that these tumors may be carcinoids, similar to the so-called carcinoma of the appendix. I would suggest that all members who have similar cases submit slides to the Chest Tumor Registry of our Association for study by different pathologists. This may clear doubtful points and make possible a report at one of our subsequent meetings with conclusive evidence of what we are dealing with.

DR. EDWARD D. CHURCHILL.—When we speak of carcinoma of the lung at the present time, we are being little more specific than were we to use an all-inclusive term such as brain tumor. I think Dr. Graham's very excellent classification, irrespective of the light of future knowledge, is a real contribution toward clarifying this subject.

Two or three of the members mentioned benign tumors of the bronchus—a subject in which we have been intensely interested. The case that I reported at Ann Arbor two years ago as carcinoma must be classified with this still undefined group of tumors.

I have had three cases of total pneumonectomy, two of the right lung and one of the left. In all cases the pleural cavity has been closed without drainage and without a thoracoplasty. Two of the patients made operative recoveries and were discharged from the hospital; the other one died on the tenth day of perforation of multiple acute duodenal ulcers. One of the surviving patients died of metastases.

In closing without drainage and without a thoracoplasty what happens to the pleural cavity? My first patient returned two and a half months after a total right pneumonectomy and died of widespread metastases. The pleural cavity at autopsy held but 250 c.c. of sterile, straw-colored fluid. Part of the obliteration, without doubt, was due to the thickening of the pleura from the carcinoma, but most of it was because of the falling in of the chest wall and the rise of the diaphragm and the shift of the mediastinum.

There was one technical step that I found helpful in a carcinoma of the lower lobe, intimately adherent to the diaphragm. It could not be ascertained whether the adhesions to the diaphragm were inflammatory or actual invasion of that organ. The adherent area was excised with the lobe carrying the resection of the diaphragm back to the vena cava. This gave a rapid mobilization of the tumor without going through the area of invasion.

The subject of metastasis in the lung from a hypernephroma has been mentioned. It must be remembered that hypernephroma is a tumor in which it is justifiable to remove a solitary metastasis, and this I have done from the lung after removal of the primary tumor. So even if the removal of a lung metastasis were done before the primary tumor could be discovered, I should consider it good therapeutics.

MR. A. TUDOR EDWARDS.—I have very little to add to what I have said except to say that one is interested in the attempts at classification. It has been a problem. These malignant lung tumors vary not only in different individuals, but in the same individual, in different parts of the tumor. I think that accounts for the great pathologic variation reported.

I should like to add that I agree with what Dr. Churchill has said on the question of the occasional possibility of successful operation on a single secondary deposit in the lung. The tumor in one of the cases described in my earlier remarks was of that type, the history commencing in 1905 when a myeloma of the fibula was operated upon. Further developments occurred in 1921 which eventually necessitated the removal of the patient's leg. In 1927 she had a small hemoptysis, and a tumor was found radiologically in the left upper lobe. This was treated by subtotal lobectomy, and the patient is still alive and well six and three-fourth years after operation. Such a case, in my opinion, does justify the occasional removal of a secondary deposit of the lung.

DR. EVARTS A. GRAHAM.—I was tremendously interested in Mr. Edwards' splendid paper. I am sorry he did not have time to present all of it. I feel, myself, that we are very greatly honored to have him come here and talk to us.

Going down the list of the other papers, I come next, of course, to Dr. Neuhof's. I am at a loss to understand what seems to be such a total difference of opinion about this matter of the malignancy of tumors depending upon their positions. I recall, however, in a recent visit to Mount Sinai Hospital that Dr. Neuhof showed me a specimen from a man who had lived for seven years with a tumor of the major bronchus. I have had one patient who lived for five years with a tumor of the major bronchus after it was diagnosed by biopsy, and I have heard of a number of others who have lived for periods of approximately that long. If the tumors in this region are as malignant as I understood Dr. Neuhof to consider them, it is difficult for me to reconcile the fact that those patients who have lived the longest invariably have had tumors in the major bronchi. I am not referring to patients who live for two years, or something of that sort, I am referring to those living for a long period of time.

However, this, of course, should not be a matter of argument, but rather a question of finding out what the facts are. I think that we shall have to let the matter wait until further facts can be obtained.

DR. HAROLD NEUHOF.—In view of the fact that the discussion has concerned the presentation of Dr. Graham's group as well as our own, it is necessary to point out briefly that there is not the discrepancy which at first sight appears to exist between Dr. Graham's presentation and our own. Dr. Graham states that he cannot understand the viewpoint we have taken and calls attention to the fact that on a recent visit to Mount Sinai Hospital we showed him an instance of cancer of the

main bronchus of seven years' duration. He states that this hardly fits in with the picture we have given of widespread metastases with carcinoma of the main bronchus as compared with limited metastases in certain types of peripherally placed carcinomas. The point is that this case was shown to him as an exceptional type of slowly growing tumor with prolonged survival without any significant therapeutic measures.

In our paper we did not take up the question of duration of life in relation to tumors in different parts of the lung. This is, in fact, a separate question and is hardly to be related to the question of the degree of malignancy. In one instance a primary tumor may have existed but a relatively short period of time, and death may have been due to a metastasis in some vital area. On the other hand, we have had instances in which patients have lived for relatively long periods of time, and then their lives terminated because of some distant metastasis, such as a cerebral focus. One can add at once that the same type of cerebral metastasis may terminate a patient's life at an early stage in the symptomatology of carcinoma of the lung. Essentially Dr. Graham's presentation deals with microscopic appearances and with the behavior of the tumors in accordance with their microscopic characteristics. The fact that the patients with main bronchus tumors in his series lived longer than those with small bronchus tumors does not mean to me that one group was more malignant than the other unless one notes what terminated life in these various groups of cases.

We should like to stress again the fact that the parenchymal and peripheral localized types which we have described as being characterized by late and limited metastases, comprise instances in which such patients did not die of the carcinoma of the lung, but died perhaps years later of distant metastases, chiefly cerebral lesions. In other words, these metastases were carried to distant areas by way of the blood stream. Indeed in not a few of these instances the primary tumor of the lung was not known to have been present because it produced so few, if any, symptoms. It is therefore obvious that a classification of the degree of malignancy on the basis of duration of life is not one which can be readily made when dealing with carcinoma of the lung.

We were glad to note in the discussion by Dr. Churchill that the point we have made, or rather the point made by Drs. Wessler and Rabin on benign tumors of the bronchus, has received some attention. Whether one refers to such tumors as carcinoids or as adenomas is relatively unimportant. The important fact is that benign tumors of the bronchus are by no means rare, that they have frequently been confused with carcinoma of the bronchus, and that the type of therapy which might be employed for malignant tumors of the bronchus has no place in the treatment of the benign tumors. Excellent results have been obtained in the group of cases reported by Wessler and Rabin by simple bronchoscopic measures.

Returning to the presentation of our material, it should be pointed out again that we were not concerned with the question of duration of life, but that our essential purpose was to demonstrate that there is a group of cases, roughly about 25 per cent of the total number of cases of carcinoma of the lung, in which the tumor is in circumscribed form in the parenchyma or in the periphery. It is only in these cases that limited or no regional metastases are to be found at autopsy. It seems to me that the important thing is to recognize that this group of cases exists and that it logically offers by far the best chances for worth-while results by operative excision. Dr. Churchill points out that in one case he sacrificed a portion of the diaphragm. That is the type of case to which I refer. In two of the five cases I reported this morning, such wide excision of the diaphragm was carried out. In other words, the tumors were peripheral ones which were peripherally invasive and not centrally invasive. In such instances one not only can, but should make what-

ever sacrifice may be necessary of parietes because it is chiefly in this direction that the carcinoma spreads. When it comes to the parenchymal tumors (and again we wish to point out that when we refer to parenchymal tumors we do not mean that they are derived from the alveoli but that they are situated in the parenchyma and are apparently unrelated to the small bronchi in the parenchyma), it should be repeated that they grow by progressive expansion rather than by invasion. In any event, these tumors lend themselves to radical extirpation.

In closing I would say that we have analyzed our material carefully and have studied it over a long period of time. The fact is that of the 100 cases which came to autopsy the main bronchus tumors, that is the tumors which can be, by and large, visualized bronchoscopically, are characterized by extensive lymph node metastases. The widespread metastases of these tumors, which comprise about three-quarters of the cases, are in striking contrast to the limited or absent regional lymph node metastases associated with the tumors which we have termed parenchymal and peripheral.

DR. CHEVALIER JACKSON.—Dr. Decker mentioned a very interesting group of cases. It is extremely important, especially now, when the technic of lobectomy and pneumonectomy is improving so rapidly, to be sure that we bronchoscopists do not report to the surgeon that a lesion is carcinoma unless the tissue has been carefully studied by a pathologist familiar with the peculiar histopathology of bronchial tumors. We had one case, which we reported at the meeting of the American Medical Association at New Orleans in 1932,* that fell into this group of tumors that have been called "carcinoids." Dr. Ewing saw the section, and he felt that it was quite likely that the lesion would prove to be malignant. The woman has, however, been absolutely free of recurrence following bronchoscopic removal of the tumor two and a half years ago.

*Jackson, Chevalier, and Jackson, Chevalier L.: Benign Tumors of the Trachea and Bronchi With Especial Reference to Tumor-like Formations of Inflammatory Origin, J. A. M. A. 99: 1747-1753, 1932.

THE TOTAL REMOVAL OF THE RIGHT LUNG FOR CARCINOMA

Report of a Successful Case

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THERE are few accounts of the successful removal of an entire lung for malignancy. There is no previous record, to my knowledge, of the successful removal of the entire right lung for this condition. Graham and Singer[1] reported the first successful left pneumonectomy, performed on April 5, 1933, for carcinoma. Rienhoff[2] has given a preliminary report of the successful removal of the left lung for tumor in two cases. Haight[3] has recently provided a review of the brief literature on the subject of pneumonectomy. He has included a bibliography of both experimental work and attempted pneumonectomy for both suppurative conditions and malignancy. Haight adds one additional case to a list of three previously reported successful pneumonectomies for left-sided bronchiectasis. In a footnote to his article there is included a brief account of recent cases. In addition to those mentioned above, there is listed a successful pneumonectomy by Archibald and a multistage procedure for bronchiectasis of the right lung by Windsberg. Windsberg's case is the only case of right pneumonectomy on record. The operation which is the subject of this report is apparently the second successful right pneumonectomy and the first one successfully carried out for malignancy.

CASE REPORT

Mrs. A. T., aged thirty-three years, referred by Dr. John B. Hawes, II, was admitted to the New England Deaconess Hospital on October 23, 1933, because of an illness of four months' duration. The symptoms were initiated by a chill and fever. A persistent cough developed which was productive of a negligible amount of sputum. It was occasionally blood streaked. Elevation of the temperature was noted intermittently. During the greater part of the time, the patient was forced to stay in bed, and the symptoms became gradually but progressively worse. The weight fell from 113 pounds to 103 pounds. Shortly before her admission, pain in the right chest accompanied the most severe paroxysms of coughing, and at times vomiting occurred. There were no other signif-

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Read by title at the Seventeenth Annual Meeting of the American Association for Thoracic Surgery at Boston, May 31, and June 1, 2, 1934.

icant symptoms. The past medical history included no important sicknesses. The patient had been married twelve years and had two normal children. The family history was irrelevant.

Upon physical examination, a state of poor nourishment was found, and the general appearance showed the effects of prolonged illness. The expansion of the chest was equal and full. There was no alteration in fremitus. The percussion note was less resonant over the right base posteriorly. A few coarse râles could be heard over the same area, most of which cleared up on deep breathing. The heart was normal in size and was not displaced. No abnormality of the heart was discerned by auscultation. The blood pressure was 118/68; the pulse was 120 when she was at rest. The remainder of the examination was entirely negative. A tentative diagnosis of neoplasm of the lung was made.

LABORATORY STUDIES

A roentgenogram of the chest showed a round discrete shadow, 4.5 cm. in diameter in the right lung field, near the hilum. This shadow was on a level with the shadow cast by the seventh and eighth ribs posteriorly and was close to the vertebral column. An area of lesser density was found extending downward and outward from the hilum, thereby obliterating the pericardiodiaphragmatic angle. (See Fig. 1.)

A bacteriologic examination of the sputum showed upon smear, gram-positive cocci, diplococci, spirilla and fusiform bacilli. A culture of the sputum showed staphylococci, streptococci, micrococci catarrhalis and pneumococci.

The number of red blood cells was 4,500,000; white blood cells 15,400; the hemoglobin was 75 per cent (Sahli). The blood smear was normal in appearance. The blood Wassermann was negative, and complement fixation test for gonococcus was also negative.

The vital capacity was 1600 c.c. The venous pressure was 8 cm. water pressure in the right arm and 8 cm. in the left arm.

Bronchoscopy was carried out by Dr. W. B. Hoover. The left bronchi were found to be normal. Considerable thick purulent secretion was found in the right main bronchus, and a point of obstruction which appeared to be tumor tissue was found in the right lower bronchus. A specimen was taken for biopsy. Microscopic examination of this tissue showed only evidence of chronic inflammation.

PROGRESS IN HOSPITAL

During observation over a period of nine days the temperature varied from 98.6° to 104°. The pulse averaged 100 and the respiratory rate 25. Paroxysms of coughing were frequent, and hypodermic medication was required to control them. The amount of sputum varied from two to seven ounces daily.

A decision to attempt excision of the right lung for probable tumor was made regardless of the negative biopsy report. The evidence for tumor was strong. There was a history of persistent cough throughout the entire period of illness with occasional hemoptysis. There was a

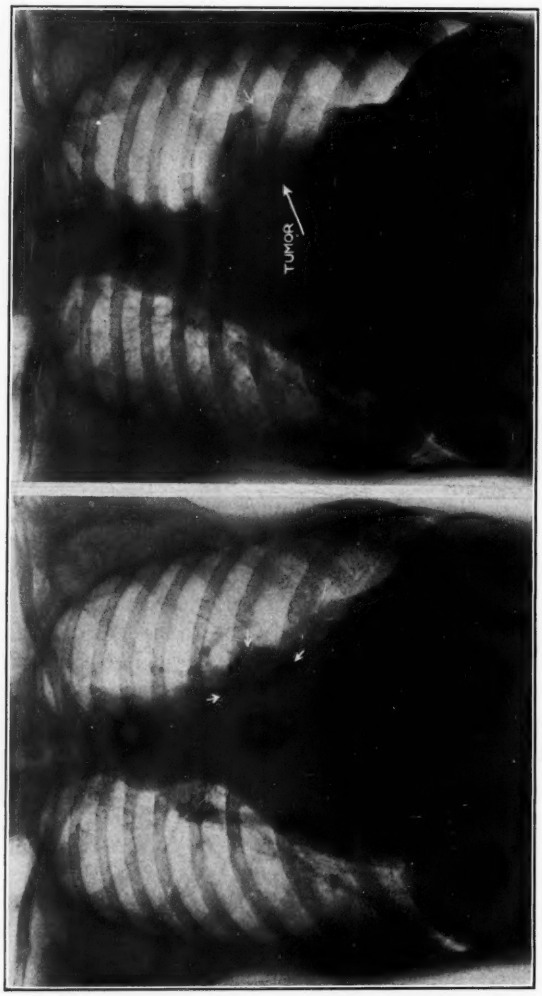

Fig. 1. Fig. 2.

Fig. 1.—Preoperative roentgenogram showing a rounded shadow in right lung field near the hilum. Below this area of density is seen a triangular shadow which was caused by obstructive atelectasis of the right lower main bronchus.

Fig. 2.—Roentgenogram after institution of pneumothorax. Note collapse of upper lobe. The circular shadow at the hilum remains in its original position. There has also been little change in the triangular area of density produced by the atelectatic lower lobe.

discrete, solid appearing roentgen ray shadow with characteristic signs of atelectasis beyond. The presence of an obstructing lesion was demonstrated bronchoscopically. Therefore, it seemed justifiable to disregard the false lead of the biopsy and prepare the patient for operation.

To produce pneumothorax, 400 c.c. of air were introduced into the right side of the chest on November 2 and further injections of 200 c.c.

to 400 c.c. of air were given at intervals of two or three days to maintain an intrapleural pressure reading of zero to minus 1 on expiration. The effect of the pneumothorax upon the temperature was favorable; after four days, it remained normal. The amount of cough and expectoration was increased at first, then it decreased noticeably. A roentgenogram of the chest showed a complete collapse of the upper and middle lobes and partial collapse of the lower lobe. The shadow of the tumor near the hilum could be seen curving outward from the dense shadow of the remainder of the collapsed lower lobe, and it was denser than the shadow cast by the collapsed upper and middle lobe. (See

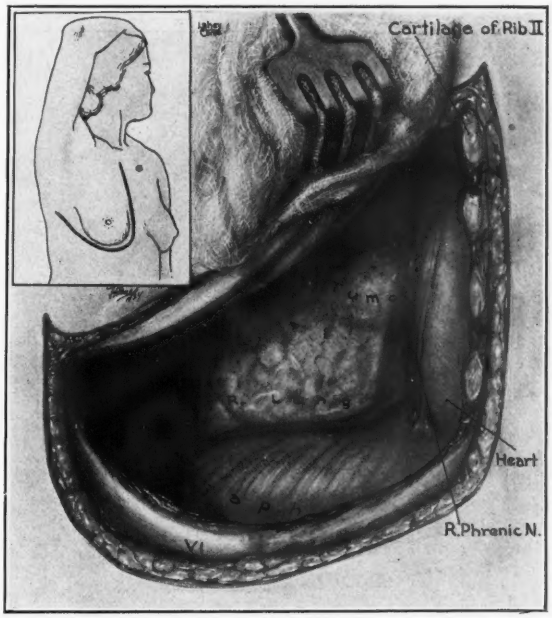

Fig. 3.—Drawing made at the time of operation. Insert shows the location of the incision in the anterolateral aspect of the chest. The inferior angle of the incision was carried down in the fifth interspace and then upward parasternally. The cartilages were severed with a scalpel. Bone cutting instruments were not necessary in providing this exposure. Adequate room in which to work was provided. Adhesions between the base of the lung and the diaphragm were separated under direct vision without difficulty. By retracting the anterior portions of the ribs, it was possible to carry out the work at the lung root satisfactorily.

Fig. 2.) An electrocardiogram taken after pneumothorax had been instituted showed a tendency for right axis deviation but otherwise it was normal. The vital capacity, after the establishment of pneumothorax was 950 c.c.

OPERATION

Eleven days after the pneumothorax was started, the operation was carried out. The patient was placed on the posterolateral aspect of the

left side and was supported so that the right axilla and entire right anterior thorax were exposed. Connections were made to provide for an electrocardiographic record during the course of the operation. The anesthesia was given by Dr. Lincoln F. Sise. Cyclopropane gas was administered using the intratracheal closed circuit rebreathing method with carbon dioxide absorption. An anterolateral incision was made which provided an incision in the fifth interspace from the posterior axillary line to the sternum, then upward parasternally, dividing the cartilages of the fifth, fourth, third, and second ribs consecutively. An excellent exposure of the right pleural cavity was obtained. Respiratory

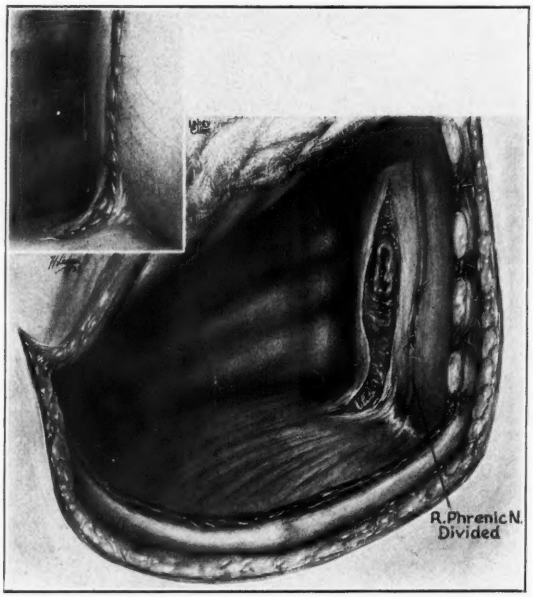

Fig. 4.—Drawing made at the time of the operation showing the appearance of the chest after the lung had been removed and the stump closed. The insert shows the manner in which the bronchial stump was completely covered by mediastinal pleura. The wound was closed without drainage, leaving the entire right hemithorax covered on its interior surface with pleura.

movements were slow and quiet. No change was noted upon opening the pleural cavity. The mediastinum was mobile. Palpation of the lung revealed a tumor near the hilum about the size of a golf ball. *No enlarged glands could be palpated in the adjacent mediastinum.* The upper and middle lobes of the lung were completely collapsed. The lower lobe was quite solid and partially adherent to the diaphragm. A drawing of the field of operation at this stage is shown in Fig. 3. Adhesions between the lower lobe and the diaphragm were separated by sharp dissection. The inferior pulmonary ligament was divided from

below, upward as far as the hilum. The mediastinal pleura was then divided entirely around the hilum. Traction upon the lung itself elongated the denuded hilar root of the lung so that application of two tourniquets was facilitated. The medial tourniquet was placed as far centrally as possible to include only the right main bronchus. Four long handled, right angled hemostatic clamps were used to anchor the tissue between the mediastinal tourniquet and the lung tourniquet. The hilum was divided with a scalpel and the lung removed. The stump of the hilum was cauterized with phenol and neutralized with alcohol. Multiple silk sutures were used to close the end of the bronchus, and

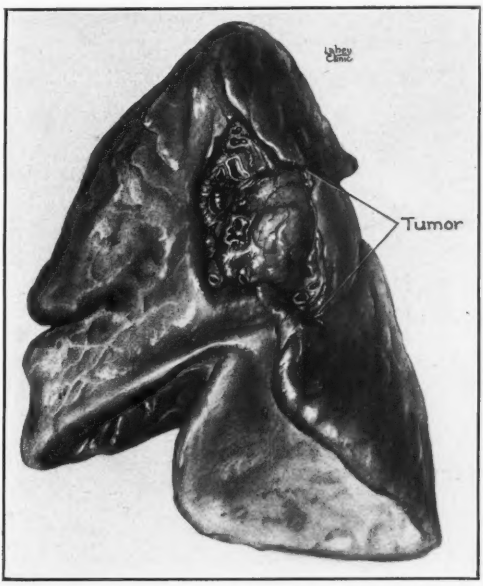

Fig. 5.—Drawing of removed specimen showing the discrete tumor bulging toward the mediastinal surface of the lung. The right lower main bronchus was completely occluded by tumor growth. There was partial occlusion of the middle and upper bronchi by the same growth. The lesion seemed to be entirely encapsulated. Lymphatic glands on the removed specimen did not show evidence of tumor extension. From the appearance of the gross specimen, it seemed probable that all of the primary lesion had been completely excised.

the vessels were ligated separately. The stump retracted into the posterior mediastinum. The edges of the mediastinal pleura were then brought together over the stump with a continuous catgut suture. This left all surfaces of the interior of the right thorax covered with pleura. In Fig. 4 is shown a drawing made at the time of operation to illustrate the appearance of the right pleural cavity at the time of closure. A drawing of the removed specimen is shown in Fig. 5. The lesion appeared to be circumscribed and was covered on the mediastinal surface

by 0.5 cm. of collapsed lung tissue. No lymphatic glands were found between the lesion and the divided hilum.

The phrenic nerve was dissected free from the pericardium about 6 cm. above the diaphragm and was divided. Two centimeters of the nerve were excised. The pleural cavity was then flushed out with saline solution and all the fluid removed by suction. The wound was closed by suturing the ribs back in their original position. The skin was closed with interrupted silk sutures and Michel clips. Drainage was not employed. A vaseline gauze air-tight dressing was applied.

The operating time was one hour and forty-five minutes. At the beginning of the operation, the pulse was 120 and the blood pressure 120 systolic and 80 diastolic. At the conclusion of the procedure the pulse

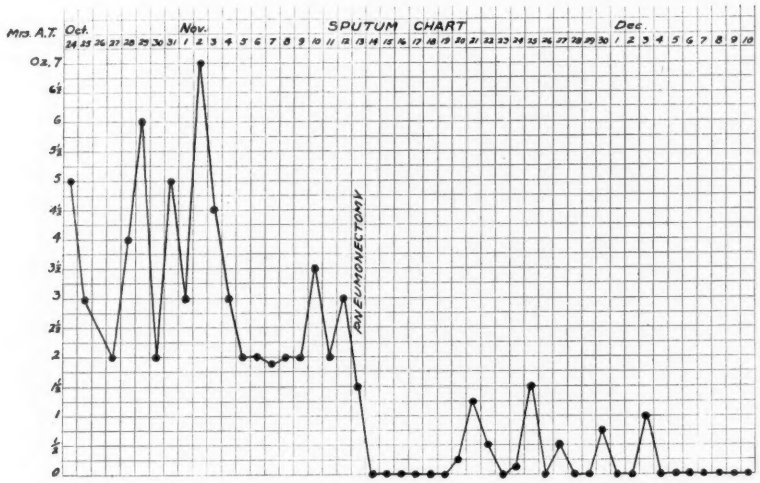

Fig. 6.—Hospital sputum chart showing copious expectoration up until the time that the lung was removed. From then on the amount of cough was negligible. The patient was entirely relieved of cough and expectoration before discharge from the hospital.

was 118 and the blood pressure was 80 systolic and 60 diastolic. Electrocardiographic tracings showed little variation during the course of the procedure, but extrasystoles were noted at the time the tourniquets were applied to the hilum. There was no change in the rate or in the quality of the pulse, at this time, however.

An important point in the management of the anesthesia should be mentioned. When work on the root of the lung was being carried out Dr. Sise produced a willful cessation of respiration. He induced apnea by over-oxygenation until respiratory movements stopped. Gentle and minimal inflation and deflation of the left lung were carried out artificially by manipulating the bag on the closed circuit rebreathing apparatus. The stopping of all respiratory movements on the part of the

patient greatly facilitated the treatment of the lung root. Apnea was maintained in this case for a period of forty-five minutes. When the bronchus had been closed off and buried in the mediastinum, natural breathing was reestablished by running carbon dioxide into the circuit.

POSTOPERATIVE COURSE

The patient was placed in an oxygen tent and kept there for a period of four days. For three days, there was no elevation of temperature; the pulse ranged between 105 and 120. The respiratory rate averaged 30. The patient did not raise any sputum and did not cough. Readings of the intrapleural pressure were taken every other day, and air was

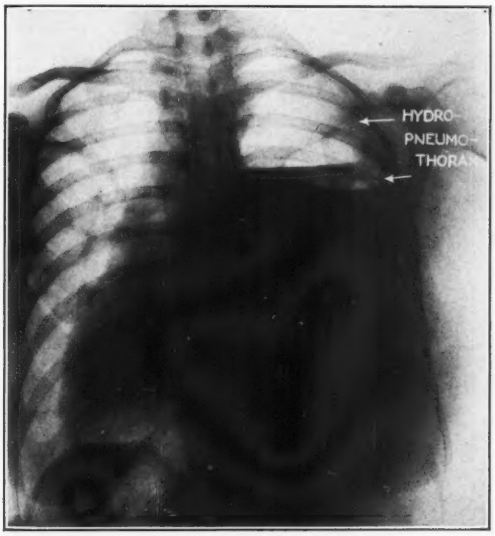

Fig. 7.—Postoperative roentgenogram taken two weeks after right pneumonectomy. Note slight displacement of heart and mediastinum to the left and the presence of a hydropneumothorax on the right side. Two weeks later the patient developed a small fistula in the upper anterior portion of the wound.

given or withdrawn to maintain a pressure between minus 2 cm. and minus 6 cm. of water. Upon the second thoracentesis, thin slightly reddish fluid was aspirated and replaced by air. Throughout the next three weeks, the temperature rose to 99° and 101° in the afternoon. The pulse remained at a rate near 100. A slight cough returned a week after operation and was productive of one-half ounce of sputum. After the seventeenth day, the cough and expectoration entirely disappeared. The hospital chart showing the amount of sputum is shown in Fig. 6.

A roentgenogram of the chest showed some displacement of the heart to the left with evidence of thickened pleura throughout the boundaries of the right hemithorax. A roentgenogram taken two weeks after op-

eration is shown in Fig. 7. Air and multiple fluid levels could be seen. Culture of pleural fluid removed three days after operation showed *Staphylococcus albus* to be present. A culture of the fluid removed three weeks later showed no growth, although the smear showed

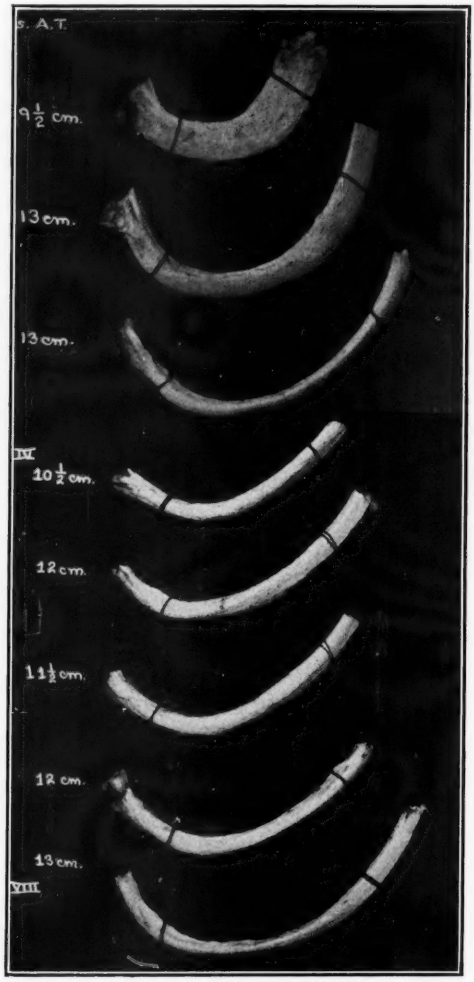

Fig. 8.—Photograph of rib segments removed to collapse right hemithorax. Ribs one to three were resected at the first-stage thoracoplasty operation. Ribs four to eight were resected at the second-stage thoracoplasty operation.

gram-positive cocci in clumps. Four weeks after operation, a fluctuant area appeared in the upper angle of the wound beside the sternum, and a small fistula developed which drained intermittently. The remainder of the wound was solidly healed.

The general condition of the patient improved steadily from the time of the operation, and she was discharged from the hospital forty-one days after operation. At this time, she was symptom free except for the draining thoracic sinus and for an occasional afternoon fever.

In order to obliterate entirely the space created in the right hemithorax, a thoracoplasty procedure was subsequently planned. The closure of this space seemed desirable for two reasons. In the first place, the thoracic sinus would probably not close as long as there was a space with contents present. In the second place, there was absorption with toxic effects of material from the cavity as evidenced by occasional elevations of temperature, leucocytosis, and a failure to regain strength.

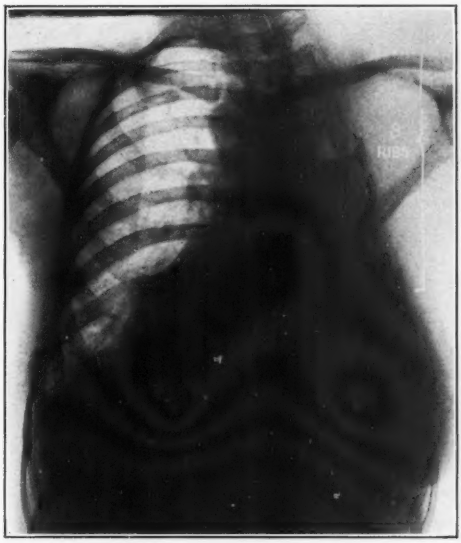

Fig. 9.—Postoperative roentgenogram after second thoracoplasty showing obliteration of right thoracic cavity. The ninth, tenth, and eleventh ribs were not resected because a previous phrenic nerve paralysis had caused sufficient elevation of the diaphragm to obliterate the basal portion of the cavity. A dense elongated shadow can be seen at the lower portion of the collapsed area which was produced by lipiodol injection of the thoracic sinus. The thoracic sinus spontaneously closed two weeks after the patient left the hospital following the second thoracoplasty so that further collapse therapy was unnecessary.

On January 10, 1934, the patient was readmitted to the hospital, and two days later a right upper thoracoplasty was done under cyclopropane anesthesia. A posterior incision was made. All of the first two ribs and one-half of the third rib were excised. Convalescence was uneventful. Drainage from the sinus became noticeably less in amount. The patient left the hospital on February 1, eighteen days after the operation.

The patient was readmitted for the second and final thoracoplasty on February 23. At this time, long segments of the fourth to the eighth

ribs consecutively were resected. Fig. 8 shows the length of ribs removed at both operations. The sinus discharged copiously for a time after the second operation, then stopped altogether. Three weeks after the last operation, the sinus was injected with lipiodol, and a small tract was outlined between the mediastinum and the dome of the diaphragm. Further rib removal was deemed unnecessary. The patient left the hospital on March 18. The opening of the sinus healed over shortly after discharge and has remained closed to the present time.

Fig. 9 is a roentgenogram of the chest made after the second thoracoplasty, showing the extent of the collapse produced by the resection of 8 ribs. Fig. 10 shows photographs of the patient just before her discharge from the hospital after the second thoracoplasty.

Fig. 10.—Photograph of the patient after second thoracoplasty shortly before leaving the hospital. Note position of pneumonectomy incision in the anterolateral aspect of the right chest. At the time this photograph was taken all the wounds were firmly healed except the upper angle of the anterior incision, from which there was a slight discharge. This sinus discharged slightly for two weeks after the patient left the hospital and has remained firmly healed since that time. Note absence of deformity and state of nutrition after going through three major surgical operations.

The patient was reexamined on May 5, 1934. She reported that she was able to be up all day and do part of her housework. She complained of inability to abduct the right arm completely and of dyspnea on exertion, but did not have any other symptoms. There was no cough and no expectoration. There were no digestive disturbances. Her weight had increased from 87 to 91 pounds. Examination showed improvement in her color and general appearance. There was no cyanosis. The pulse was 108, and the temperature was 98.2°. The anterior and posterior wounds were firmly healed. The anterior thoracic sinus had entirely closed. The heart was in the midline. The vital capacity was 1,150 c.c.

PATHOLOGIC REPORT

The following pathologic report was made by Dr. Shields Warren.

"The specimen consists of a right lung weighing 315 gm. At the hilus of the middle lobe is a moderately firm, slightly resilient, definitely circumscribed tumor mass 4 cm. in diameter. The tumor tissue fills one of the main bronchi and compresses the surrounding lung tissue. The bronchioles are markedly dilated and filled with mucoid material. The lung tissue is collapsed and moderately firm."

Histologic examination: "There is relatively little invasion of the surrounding tissue. The cells are arranged in anastomosing strands from 2 to 8 cells wide with a fair amount of hyalin. The stroma is moderately vascularized. The tumor cells are principally columnar in shape, relatively small, and ill defined. The cytoplasm shows basophilic

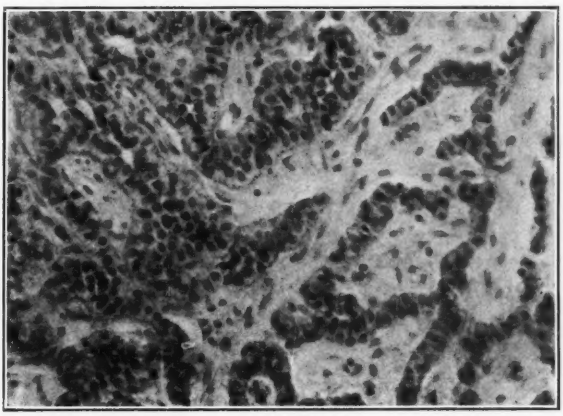

Fig. 11.—Microphotograph of tumor removed. Note anastomosing strands of columnar cells. The nuclei are moderate in size and hyperchromatic and usually oval. Mitoses are rare. There is little invasion of the surrounding tissue. Diagnosis: Carcinoma, probably of bronchial origin. See text for controversy over nature of tumor.

staining and with the silver stain shows argentaffine granules. The nuclei are moderate in size, hyperchromatic and usually oval. Mitoses are rare. Microscopic diagnosis: Carcinoma, unclassified." (See Fig. 11.)

A record of the case and microscopic slides were sent to the Thoracic Tumor Registry. Their report follows:

"Further sections have been kindly supplied by Dr. Shields Warren. These were stained in this laboratory by the Masson trichrome lichtgrün method, by Mallory's phosphotungstic acid hematoxylin method, and with the mucicarmin stain. None of these shows anything of note. There is no mucus in the cells of the tumor, which would appear to rule out bronchogenic origin. Sections impregnated with silver by the

Masson-Fontana and the Foot and Foot methods show a small number of argentaffine granules throughout the tumor, and the latter method reveals a number of typical argentaffine cells such as have been described by Masson in his articles on carcinoid. These facts, coupled with the morphology of the tumor, particularly as regards its nuclear structure, make it seem almost certain that we are dealing with a carcinoid, probably metastatic from the bowel. The only alternative would be some tumor of the chromaffin system (possibly adrenal), in which case the presence of argentaffine granules is anomalous.

"Diagnosis: Carcinoid, metastaic to the lung, possibly from a primary site in the bowel." By Dr. N. C. Foot of the Committee on Thoracic Tumors of the American Association for Thoracic Surgery.

Dr. Shields Warren has reviewed the slides and still considers the lesion a primary lung tumor, probably of bronchial origin. He admits the presence of cells taking the silver stain but does not believe the tumor to be a metastatic lesion from a carcinoid tumor of the intestine.

COMMENT

There are several factors in this case that warrant emphasis.

1. Pneumonectomy was carried out even though a bronchoscopic biopsy was negative for malignancy. The operation was done because the history and the x-ray examination furnished strong evidence for the diagnosis of tumor of the lung. The roentgenogram showed a discrete shadow near the hilum with an associated shadow typical of atelectasis resulting from bronchial occlusion. It would seem that if malignancy of the lung is to be attacked in its early stage, a positive bronchoscopy specimen should not be insisted upon. It is logical to assume that the incidence of success in securing a positive biopsy bronchoscopically in malignancy of the lung will not be greater than the incidence of positive results in proctoscopic biopsies in rectal cancer. Yet, the bronchoscopic examination was valuable, since it showed that the occlusion of the bronchus was not due to a foreign body.

2. The maintenance of a fairly complete pneumothorax before operation is of tremendous value from four points of view: (1) Preliminary collapse of the involved lung permits accommodation of the contralateral lung for carrying on the entire respiratory function. (2) It permits the adjustment of the circulation in the two lungs well in advance of the ligation of the pulmonary vessels. (3) It permits gradual deflation and emptying of the affected lung of its secretions and removes the danger of a spillover of material into the contralateral lung, at the time of operation. (4) Previous collapse of the lung is of advantage technically in that the lung is handled more easily and a knowledge of the location of adhesions can be obtained in advance of the operation.

3. Safe, controllable anesthesia is essential. An intratracheal tube and a closed circuit inhalation anesthesia with carbon dioxide absorption

provided absolute control of respiratory activity in the case reported. Cyclopropane gas anesthesia was chosen because it can be given in concentrations as low as 5 to 15 per cent and therefore permits the administration of 85 to 95 per cent oxygen during the course of the surgical anesthesia. This high percentage of oxygen results in shallow, quiet respiratory movements with minimal effort on the part of the patient. The use of the apnea technic to produce complete cessation of respiratory movements is of distinct advantage when working upon the root of the lung.

4. The removal of the lung in one stage and closure of the chest without immediate thoracoplasty has two advantages: (1) The pathologic condition is immediately removed. The patient is not required to suffer the ill effects of the lesion itself while recovering from the first-stage operation. The danger and consequences of infection in the involved lung are removed. The danger of a bronchiogenic spread of material into the uninvolved lung is also removed. (2) With a closed and rigid thorax, pressure against the mediastinum and heart can be controlled with intrapleural pressure readings and instillation or withdrawal of air as indicated. If a partial thoracoplasty is done at the time that the lung is removed, the flaccid chest wall disturbs the pressure relationships and makes control of the intrapleural pressure more difficult and uncertain. By the method described here which was also employed by Rienhoff, the mechanics of the chest are altered but little. The patient starts with a complete pneumothorax plus the collapsed lung and ends up with a complete pneumothorax without the collapsed lung. The mechanics of the thoracic cage itself are not disturbed by the one-stage operation which removes the lung at that time.

5. The necessity of subsequent thoracoplasty will vary with individual cases. In Rienhoff's first case, the patient was a child. In a young patient, the contralateral lung is likely to expand to fill the entire hemithorax. The necessity of subsequent thoracoplasty is also determined in part by subsequent bronchial fistula or infection in the pleural space. In the reported case, an obliteration of the space which was infected seemed desirable. The same policy is followed for tuberculous patients with intrapleural infection, following pneumothorax treatment, since recovery does not occur until the space is obliterated. In the case under discussion, fever and weakness resulted from absorption from the right pleural cavity. When the space was obliterated, the sinus closed, the temperature became normal and the patient was restored to relatively good health, excepting for the limitation of respiratory reserve.

6. The problem in pneumonectomy for bronchiectasis or malignancy when the pleura is adherent is quite different from that found when the pleura is free and preparation by pneumothorax is possible. When the lung can be collapsed in advance by pneumothorax, I see no object in dividing the actual operation of pneumonectomy into stages. Prelim-

inary thoracoplasty has been carried out in bronchiectasis cases. Alexander and Haight prefer to ligate the pedicle and permit the lung to slough within the chest. This, to me, seems undesirable. When the pleura is adherent, however, the problem is changed completely. Under these circumstances, there may be greater safety in a two-stage operation, the first consisting in the separation of adhesions and the second in the amputation of the lung.

SUMMARY

1. A successful right pneumonectomy for carcinoma is reported in detail.

2. The importance of a period of preparation by pneumothorax is stressed.

3. The value of anesthesia with a high concentration of oxygen and the use of the apnea technic are commented upon.

4. The necessity of subsequent thoracoplasty is discussed.

A second successful pneumonectomy for carcinoma of the lung was done by the author on May 2, 1934. The lesion was situated at the bifurcation of the primary left bronchus, necessitating the entire extirpation of the left lung. The patient, a woman, aged forty-five years, was prepared three weeks prior to operation by pneumothorax. At the present time, four weeks after operation, the wound is firmly healed without fistula formation and fluid aspirated from the left pleural cavity is sterile upon culture. Subsequent thoracoplasty is contemplated. The details of this case will be reported later. Small pneumothorax refills are being given at infrequent intervals.

NOTE.—A recent follow-up examination of the two patients mentioned in this report one year and six months after operation, respectively, found them perfectly well, without symptoms and free of any signs of metastasis.

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LOBECTOMY FOR CARCINOMA OF THE LUNG*

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THORACIC surgery has made tremendous progress during recent years, so much so that at times fear has been expressed lest we are advancing too rapidly. On closer inspection we find that the greatest share of this progress is due to bringing pulmonary tuberculosis within the domain of surgery and to the more radical treatment of pulmonary suppuration than was formerly employed. One of the major problems still confronting us is the treatment of malignant tumors of the lung. Progress in this field has been slow and continues so. The chief reasons for this seem to be the difficulty in making an early diagnosis and the technical or supposedly technical difficulty of performing lobectomy. There is no doubt in the mind of many thoracic surgeons that a lobe, or even an entire lung, may be safely removed if the diagnosis is made before the primary growth has become attached to or has involved the surrounding organs, and so long as the main bronchus is free of disease. There is much to be learned concerning the onset of malignant tumors of the lungs and bronchi, their progress, their invasive qualities, their pathology and their radiosensitivity. To bring this about, the interest of medical men and of the various specialists concerned must be aroused.

It is therefore timely that our Association should at this meeting discuss the subject of lobectomy and pneumonectomy in the hope that the information collected in this way may aid in the progress toward combating this treacherous condition. It is in this spirit that I venture to report a single case of carcinoma of the lung in which I recently performed a lobectomy.

Mrs. T. G., forty-five years of age, was admitted to the Lenox Hill Hospital, January 3, 1934, after a period of preliminary observation at another institution. She brought with her several x-ray plates showing the progress of an intrapulmonary lesion, as well as records of laboratory examinations pointing to a possible malignant condition of the left lung. Her chief complaints were pain in the left chest, bloody expectoration, dyspnea, and night sweats. She had had symptoms for six months. In July, 1933, she contracted what she called a "cold," followed a few days later by a little bloody expectoration. She placed herself under medical care and had x-ray examinations made of the chest, but did not improve. (Fig. 1.) In addition to bloody expectoration she had in the

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course of months developed dyspnea, weakness, night sweats, and lately also pain in the chest. A recent chest aspiration had brought temporary partial relief.

There was nothing in the past or family history relating to her present symptoms. She had always enjoyed excellent health, and did not look particularly ill when admitted. She was well developed and weighed 125 pounds. Temperature was 100°, pulse 96, and respiration 20. General examination showed nothing definitely abnormal. Chest examination showed dullness over the lower two-thirds of the left chest with absent fremitus and breath sounds. The opposite side seemed normal, and both apices were clear. The heart was not appreciably displaced, and no evidence of disease was noted.

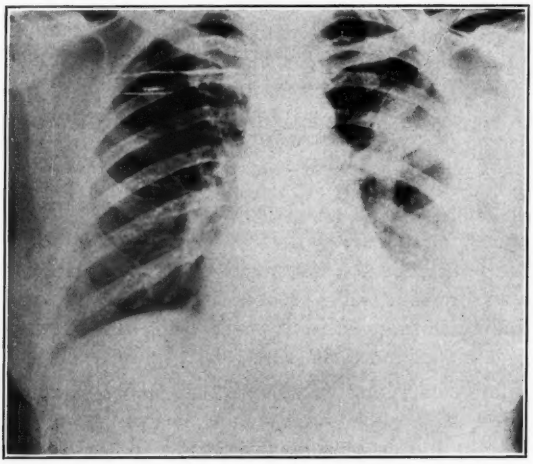

Fig. 1.

The physical signs pointed to a pleural effusion, while the history indicated an intrapulmonary lesion. It was decided to aspirate and examine the pleural fluid, to induce a moderate pneumothorax and then to repeat x-ray examinations, to examine the sputum, and to have a bronchoscopy done. Observation in the meantime showed that we were dealing with an afebrile condition, that she had a normal blood count, normal urine, and a negative Wassermann.

Roentgen ray examination after the aspiration of 1,100 c.c. of clear straw-colored fluid, followed by the injection of 300 c.c. of air did not give the desired information. Another aspiration of 1,100 c.c. was therefore done a few days later, and an x-ray examination then showed only a small amount of fluid still present at the left base. The heart was considerably displaced into the right chest. The left lower lobe was nearly completely collapsed, while the upper lobe was prevented from

complete collapse by dense bands of adhesions as well as by an intrapulmonary focus, which apparently showed cavity formation. (Fig. 2.) From an x-ray standpoint there was strong likelihood that the lesion was a suppurative one, though it was recognized that the presence of a pleural effusion pointed to malignancy.

Examination of the sediment obtained by centrifuging the fluid showed fibrin, in the meshes of which were found numerous round cells of the lymphocytic type together with many larger mononuclear cells, probably of connective tissue origin. There were also present a number of eosinophilic leucocytes and here and there large protoplasmic cells of various sizes containing small or large nuclei, some of which took a rather deep basic stain. They were considered as possibly malignant cells, but a positive diagnosis could not be made. On culture the fluid was sterile.

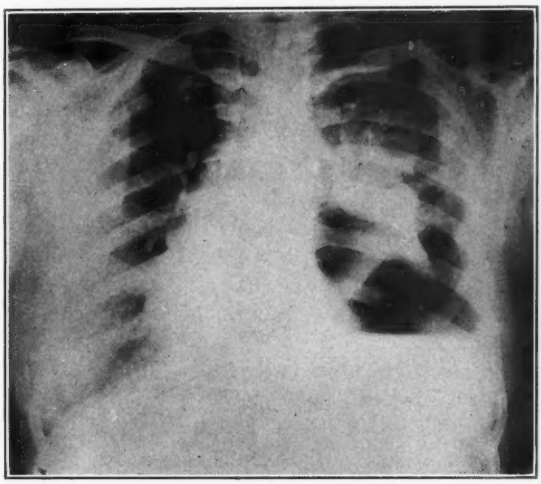

Fig. 2.

Examination of the sputum showed it to be negative for tubercle bacilli. There were no cells present which would aid in the diagnosis of malignancy.

Bronchoscopic examination showed no distortion of the trachea. The upper portion of the left main bronchus was sharply angulated and slightly narrowed by compression from without. A biopsy was taken from a small mass of granulation tissue, and later reported negative for malignancy. The bronchoscopist was of the opinion that we were probably dealing with a malignant tumor, though a chronic abscess could not be ruled out.

The mass of information finally available to us, consisting of a good history, x-ray examinations covering the entire period, and laboratory

findings obtained since admission, pointed to an intrapulmonary focus with a secondary pleural effusion. The nature of the lesion could not be definitely stated even after a period of observation lasting six months.

We made a clinical diagnosis of probable malignancy of the lung, based on the gradual onset with bloody expectoration, the afebrile course, increasing dyspnea, and finally pleural effusion, even though we had no positive support from the roentgenographic, bronchoscopic, or laboratory departments.

Operation was advised in the hope of being able to do a lobectomy. This hope was strengthened by the bronchoscopic observation that apparently no tumor had invaded the main bronchus of the upper lobe and that therefore a ligation of the pedicle would be possible.

Under colonic avertin anesthesia supplemented by gas oxygen ether, an incision was made along almost the entire fifth intercostal space. The rib above and that below were divided behind the angle and the pleura was incised. There was some difficulty encountered in spreading the ribs apart because the lung was found adherent in the posterior part of the line of incision. After freeing it, the chest was opened wide and held that way with the aid of a rib spreader. Considerable straw-colored fluid was removed by suction. A collapsed lower lobe presented which was so solid that it stuck up freely into the chest. It felt like liver, and apparently contained no air at all or only very little. It was extensively adherent to the upper lobe, as well as anteriorly and posteriorly. Nothing abnormal could be felt within it. The upper lobe was less collapsed, and contained a hard, nodular tumor which was visible and palpable on its outer surface. With great difficulty, partly by blunt, and partly by sharp dissection, the two lobes were separated so completely that the pedicle of each was clearly visible. It was found that tumor tissue extended close to the main bronchus so that it was doubtful whether a lobectomy could be done in normal tissue. In addition numerous small tumor implantations were found on the lateral chest wall as well as in the pleura of the lower lobe and covering the aorta. In spite of that a lobectomy was decided on, in the hope that the metastases might be controlled by x-ray treatment.

An angular pedicle clamp was applied to what seemed to be normal pedicle tissue of the upper lobe. It was not possible to apply another clamp distal to this because of the infiltration within the lobe. The pedicle was then divided with the electrocautery knife some distance beyond the clamp but apparently in uninvolved tissue. A double suture of this tissue failed to control bleeding, and a catgut ligature had to be passed through the middle of the pedicle and tied on both sides, which effectively controlled all leakage.

The condition looked very satisfactory. An attempt was now made to inflate the remaining lower lobe, but was not successful on account of the thickened visceral pleura. Multiple incisions were therefore made in

this layer but even after that, inflation was not satisfactory. The lung had evidently undergone changes as the result of long compression by the pleural fluid. The lobe fell into place very nicely and naturally covered the stump of the upper lobe. In order to hold it there, a few chromic catgut sutures were placed. A stab wound was now made in the ninth intercostal space, posterior axillary line for the purpose of closed drainage. After inserting a half inch rubber tube, which was allowed to project into the chest for a distance of three inches, the chest wound was closed in layers. During this time the outer end of the tube was kept under fluid level and attempts were made to bring about inflation of the lung.

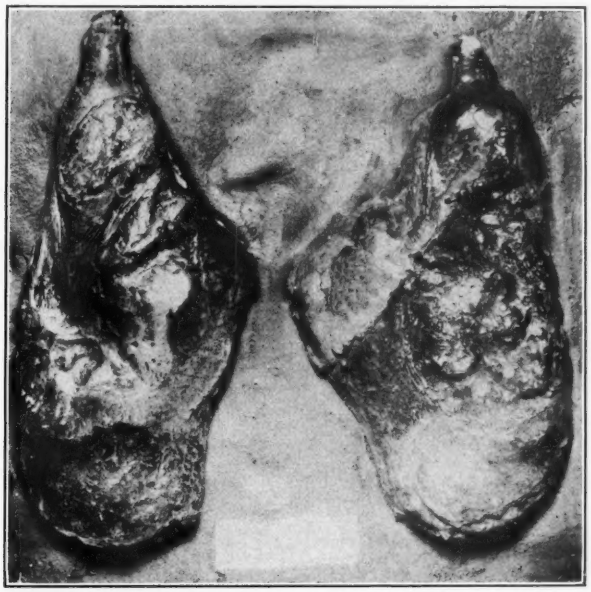

Fig. 3.—Left upper lobe containing carcinoma.

The patient stood the operation very well. She was given Ringer's solution intravenously during operation and a transfusion of 500 c.c. of whole blood immediately after. Her pulse became quite small toward the end, but there was no respiratory distress.

She reacted well during the first twenty-four hours, with the highest temperature 102.4.° The pulse was regular, 110 per minute. She had no cyanosis and no respiratory distress. There was drainage of 400 c.c. serosanguineous fluid during the first twenty-four hours. Breath sounds were present anteriorly, but sounded distant. The back was not examined. An x-ray picture of the chest taken that day showed fairly good lung expansion, with no displacement of the mediastinum.

The chest wound healed by primary union.

The drainage tube was continued, perhaps unduly long, because of fear that infection of the pleura might result from the lung pedicle, or that a bronchial fistula might form, but fortunately nothing happened.

The patient was allowed out of bed on the eighteenth day; she gained strength slowly. X-ray treatment was started four weeks after operation, but was discontinued because of the resulting severe reaction consisting of vomiting, irregular pulse, and weakness. After the drainage opening had healed, there was some intrathoracic disturbance due to incomplete expansion of the lower lobe and some fluid collection. An exploratory puncture resulted in the withdrawal of clear fluid which was negative on culture. This fluid later absorbed spontaneously.

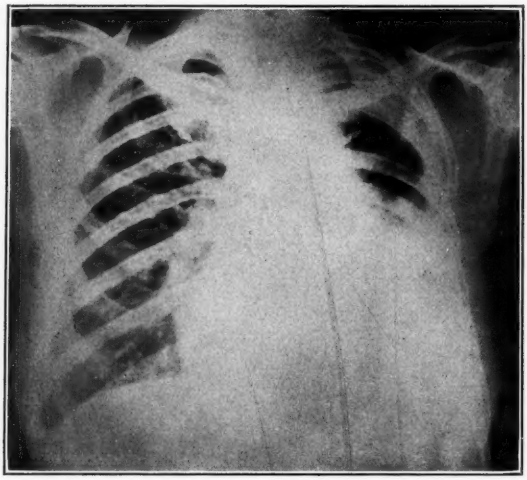

Fig. 4.

When it was considered safe to do so, x-ray treatment was again started, but the reaction which apparently resulted from it made us very cautious. After the third treatment there was vomiting, weakness, and rise of temperature to 103°, which could be accounted for in no other way. In spite of discontinuing x-ray treatments, the temperature continued high and rose to 105°. A blood count done at this time showed W.B.C. 1,500, with no polynuclear neutrophiles. We were apparently dealing with agranulocytosis. A transfusion was given at once, as well as an intramuscular injection of 5 c.c. of pentnucleotide. Careful subsequent blood studies on this patient confirmed the diagnosis of granulocytopenia. There was at no time any sore throat, or mouth or throat lesion of any sort. It was considered that the patient, or her particular tumor, was very radiosensitive and that it was the x-ray treatments which initiated the symptoms. However, she had also received allonal

and pyramidon which are at times held responsible for this condition. After several doses of pentnucleotide she recovered. Subsequent x-ray treatments were given at longer intervals and in smaller doses and were well borne.

The pathologic diagnosis of the lung tumor was "carcinoma of the lung, Grade II." (Fig. 3.)

The patient was discharged April 20, 1934, healed and in fair condition. The chest has contracted somewhat owing to the lack of power of the lower lobe to reexpand fully. (Fig. 4.)

The outstanding features of this case to which atention may be directed are:

1. The present-day difficulty of making an early diagnosis of a primary lung tumor.

2. The importance of properly evaluating early symptoms.

3. The difficulty of interpretation of early x-ray films.

4. The comparative ease with which a lobectomy may be successfully performed in a suitable patient.

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STEWART, WILLIAM H.—222 West 79th Street, New York, N. Y.
TOREK, FRANZ—1212 Fifth Avenue, New York, N. Y.
WHIPPLE, ALLEN O.—180 Fort Washington Avenue, New York, N. Y.
WILMS, J. H.—12 West 7th Street, Cincinnati, Ohio

Deceased Members

1920 KENNETH A. J. MACKENZIE
SAMUEL J. MELTZER
LEO S. PETERSON
1921 ROBERT M. BROWN
H. H. JANEWAY
ROBERT C. PATTERSON
JOSEPH RANSOHOFF
1922 HENRY L. LYNAH
1923 WILLIAM S. HALSTEAD
1927 SPARRELL S. GALE
FRED W. PARHAM
CHARLES H. PECK
1928 HOWARD A. LOTHROP
1931 NORMAN B. CARSON

1932 EMIL BECK
SELLING BRILL
CHARLES LOCKWOOD
WILLY MEYER
SIDNEY YANKAUER

1934 CARL A. HEDBLOM
ALEXIS VICTOR MOSCHCOWITZ
RAY MATSON

Past Presidents

1918 SAMUEL J. MELTZER, New York
1919 WILLY MEYER, New York
1920 WILLY MEYER, New York
1921 RUDOLPH MATAS, New Orleans
1922 SAMUEL ROBINSON, Santa Barbara
1923 HOWARD LILIENTHAL, New York
1924 CARL A. HEDBLOM, Chicago
1925 NATHAN W. GREEN, New York
1926 EDWARD E. ARCHIBALD, Montreal
1927 FRANZ TOREK, New York
1928 EVARTS A. GRAHAM, St. Louis
1929 JOHN L. YATES, Milwaukee
1930 WYMAN WHITTEMORE, Boston
1931 ETHAN F. BUTLER, Elmira, N. Y.
1932 FREDERICK T. LORD, Boston
1933 GEORGE P. MULLER, Philadelphia
1934 GEORGE HEUER, New York

Past Secretaries

1918-1922 NATHAN W. GREEN, New York
1922-1924 CHARLES GORDON HEYD, New York
1924-1929 ETHAN FLAGG BUTLER, Elmira, N. Y.

Meeting Dates

1918 Chicago, June 10
1919 Atlantic City, N. J., June 9
1920 New Orleans, May 1
1921 Boston, June 6
1922 Washington, D. C., April 29
1923 Chicago, May 28
1924 Rochester, Minn., June 5
1925 Washington, D. C., May 4
1926 Montreal, P. Q., September 30
1927 New York, May 9
1928 Washington, D. C., April 30
1929 St. Louis, April 25
1930 Philadelphia, May 12
1931 San Francisco, July 1
1932 Ann Arbor, Mich., April 18
1933 Washington, D. C., May 9, 10, 11
1934 Boston, May 31, June 1, 2
1935 New York, June 3, 4, 5

American Association for Thoracic Surgery to Meet in New York

The Eighteenth Annual Meeting of the American Association for Thoracic Surgery will be held in New York City, June 3, 4, and 5, 1935. The Waldorf-Astoria will be the hotel headquarters for the meeting.